THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—40TH YEAR SYDNEY, SATURDAY, JULY 18, 1953 No. 3

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.

Regional Non-Bacterial Suppurative Lymphadenitis and its Relationship to "Cat-Scratch Disease", by J. I. Tonge, J. A. Inglis and E. H. Derrick .. 81
Cerebral Astrocytic Gliomata, with the Report of a Case, by Irvine J. Hunter 85
The Use of Paraldehyde in Alcoholic Delirium Tremens, by Douw G. Steyn, B.Sc., Dr.Med.Vet., D.V.Sc. 91
A Summary of All Cases of Ante-Partum Hæmorrhage in the Public Section of the Brisbane Women's Hospital during the Period from July 1, 1951, to June 30, 1952, by J. F. Dunkley, M.B., B.S., and R. Thatcher, M.R.C.S., L.R.C.P., M.R.C.O.G. 93
Air Evacuation of Casualties in the Korean War, by N. M. Kater, M.C. 94
Continuous Immobilization of Joints in Rheumatoid Arthritis, by Michael Kelly 95

REPORTS OF CASES—

Granulosa Cell Tumour of the Ovary with Spread to Endometrium and Cervix, by A. R. H. Duggan 99
Aplastic Crisis in Congenital Hæmolytic Icterus (Acholuric Jaundice): A Description of Three Cases, by J. Margolis 100

REVIEWS—

The 1952 Year Book of Orthopedics and Traumatic Surgery 103
Modern Treatment Year Book, 1953 104
New Concepts of Hypnosis 104

NOTES ON BOOKS, CURRENT JOURNALS AND NEW APPLIANCES—

Family Doctor 104

BOOKS RECEIVED 104

LEADING ARTICLES—

François Rabelais 105

CURRENT COMMENT— Page.

Effects of Hæmorrhage in Man 107
The Treatment of Vesical Carcinoma 107
Commonwealth Index of Scientific Translations .. 108
The Nature of Cardiac and Pulmonary Dyspnœa .. 108
Malaria Terminology 109
The Medical Research Council of New Zealand .. 109

ABSTRACTS FROM MEDICAL LITERATURE—

Pædiatrics 110
Orthopædic Surgery 111

SPECIAL ARTICLES FOR THE CLINICIAN—

LXXI. Gall-Stone Disease 112

MEDICAL SOCIETIES—

Melbourne Pædiatric Society 113

OUT OF THE PAST 117

SPECIAL CORRESPONDENCE—

London Letter 117

CORRESPONDENCE—

The John Adey Fund 118

OBITUARY—

Hilda Josephine Gardner 118

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 119

POST-GRADUATE WORK—

North-Eastern Medical Association 119
The Melbourne Permanent Post-Graduate Committee 119
Seminars at the Royal Prince Alfred Hospital .. 120

NOMINATIONS AND ELECTIONS 120

DEATHS 120

DIARY FOR THE MONTH 120

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 120

EDITORIAL NOTICES 120

REGIONAL NON-BACTERIAL SUPPURATIVE LYMPHADENITIS AND ITS RELATIONSHIP TO "CAT-SCRATCH DISEASE".

By J. I. TONGE,

Laboratory of Microbiology and Pathology, Brisbane;

J. A. INGLIS,

Department of Pathology, University of Queensland;

AND

E. H. DERRICK,

Queensland Institute of Medical Research, Brisbane.

IN a previous publication (Inglis and Tonge, 1950) attention was drawn to a disease of unknown ætiology occurring in Queensland, producing visceral granulomatous lesions, the histological structure of which was similar to that of *lymphopathia venereum*. Three cases were described, one associated with fatal encephalitis.

During the last two years 16 cases of a peculiar regional lymphadenitis have been studied. It was found that glands from all these subjects presented the same curious histological picture seen in the visceral granulomatous lesions previously described. The clinical behaviour of the cases and the histological detail of the affected glands also presented a striking similarity to the lymphadenitis occurring in "cat-scratch fever", descriptions of which have come from France (Debré *et alii*, 1950; also Mollaret *et alii*, 1950), from the United States of America (Daniels and MacMurray, 1951; Fox, 1952), and from England (Garai, 1952; also Campbell and Wheaton, 1952).

In this group of 16 cases the disease appeared as a lymphadenitis restricted usually to one or in some cases two unilateral groups of lymph glands; suppuration occurred, but the evolution has usually been more prolonged than in pyococcal adenitis. There was no noticeable response either to sulphonamides or to penicillin, but recovery occurred without sequelæ.

Possible Relationship to "Cat-Scratch" Disease.

Our suspicion that the infection causing the lymphadenitis might be acquired from cats was aroused when a patient (Case I) volunteered the information that he had been scratched on the hand by a cat not long before he developed homolateral axillary adenitis. In view of this possible association between the cat-scratch and the onset of adenitis we made inquiries whenever possible in all cases which subsequently were investigated. The cases in our series were scattered over all parts of Queensland and, unfortunately, it was possible for us to obtain detailed histories from only a few. Of ten patients from whom a reasonably complete history was obtained, six gave a history of contact with cats, and of these, three stated that they had been scratched or bitten not long before the onset of the lymphadenitis.

About this time reports began to appear in overseas journals describing a similar type of lymphadenitis, and various names were used to describe the condition, such as *"cat-scratch disease"* and *"la maladie des griffes du chat"*. Both French and American authors described a suppurative lymphadenitis from which it was not possible to recover any causative organism. The histological picture of these glands closely resembled that seen in our own cases.

In view of the clinical and histological similarity we believe the condition observed in Queensland belongs to the same entity. Strength is lent to this conclusion by the fact that all three patients on whom an intradermal test was carried out with the "cat-scratch" antigen, supplied from London, gave a positive reaction. This antigen was prepared at the Central Public Health Laboratory from material from a case (Bensted, 1952). Our control test with this antigen gave no reaction.

Clinical Features.

In all the 16 cases under review the lesions were apparently confined to the lymph glands, and in all but one case the glandular enlargement was unilateral. In 10 of the 16 cases only one group of glands was involved. The distribution of the glands affected and the frequency of affection were as follows: axillary glands seven cases, epitrochlear four, inguinal four, posterior cervical four, submental one. In the four patients with more than one group of glands involved the distribution was as follows: axillary and epitrochlear two cases, axillary and inguinal one case, axillary and posterior cervical one case. Whenever a history of some local lesion, such as a cat-scratch, was available the affected glands were on the same side.

Most of the patients presented with glandular enlargement, usually accompanied by tenderness of varying degree. Transient fever was not uncommon, and one patient (Case I) had prolonged fever, anorexia and malaise.

The affected glands varied greatly in size from about one centimetre up to more than 10 centimetres in diameter, and in this latter case the lesions were mistaken for malignant newgrowths. It was difficult to determine the incubation period, but in Case I, in which reasonably precise details were available, the glands did not become enlarged until one month after the local lesion occurred.

Suppuration was common clinically and was seen to be present in every case on microscopic examination. The apparent failure of the lymphadenitis to respond to sulphonamide and penicillin therapy was a consistent finding. No details are available in our series as to the response to choramphenicol or aureomycin; but Daniels and MacMurray (1951) mention that aureomycin and terramycin appear to shorten the course of the disease.

In those cases for which a follow-up was available there was an uneventful recovery without sequelæ.

Pathology.

On macroscopic examination the glands either were discrete or more commonly consisted of a coalescent mass. Occasionally the tissue appeared necrotic and friable. On the cut surface pale yellowish suppuration was observed in some.

The earliest histological change appeared to consist of an accumulation of epithelioid cells in groups throughout the gland (see Figure I). When these groups had attained a variable size necrosis occurred in the centre (see Figure II), and when this necrosis occupied approximately one-third of this lesion infiltration with polymorphonuclear leucocytes occurred (see Figure III). This infiltration with polymorphonuclear cells was a striking and consistent feature giving rise to round and stellate abscesses (see Figures IV and V). These abscesses varied greatly in size, and when fully formed consisted of a mass of pus cells with a palisading of epithelioid cells and occasional giant cells at the periphery (see Figure VI). At a later stage the polymorphonuclear cells appeared to undergo degeneration. It was common to find necrotic areas in which a few degenerate polymorphonuclear cells were scattered. The lesions within the gland seem to disappear by gradual absorption and shrinkage.

Investigations as to Ætiology.

To date the ætiology of the disease is not definitely established. Most investigators overseas have had no success in isolating an ætiological agent, although several have been able to prepare an antigen from affected glands, suitable for skin testing.

Mollaret and his co-workers have probably done more to investigate the ætiology of the disease than anyone else. In 1950 they succeeded in transmitting the disease to one of four volunteer medical students after several attempts. Their technique was to inoculate and scarify the skin with pus from an affected gland. Later (Mollaret *et alii*, 1951) they were able to transmit the disease to monkeys (*Carcopithecus æthiops sabens*). They used emulsions made from infected human lymph glands, and by intracutaneous inoculation succeeded in producing a primary lesion in the monkeys at the site of injection in twenty-eight to fifty-four days, and enlarged regional lymph nodes developed in thirty-six to sixty-three days. These lesions, both local and glandular, resembled exactly those seen in man. In the same paper Mollaret and his co-workers describe having found intracellular basophilic "granulo-corpuscles" in lymph nodes, and he considers that these are a visible form of the causative agent, which he regards as being a virus. They were also able to demonstrate intranuclear and intracytoplasmic inclusion bodies, but they consider that these may well be non-specific.

No organism has yet been detected by bacteriological or mycological cultures of the lesions, and so far no one has reported any success with inoculation of the usual laboratory animals or eggs in recovering the causative organism.

Owing to the difficulty in obtaining fresh material for microbiological investigation our studies have been confined to three cases (Cases I, II and III). In these cases bacteriological and mycological cultures were made, and mice, guinea-pigs, eggs and on one occasion a kitten were inoculated without success.

The findings of Mollaret, together with the failure of other workers, including ourselves, to recover any infective agent by ordinary means points strongly to the disease being viral in origin.

Distribution of Cases.

A striking feature in our series is the widespread distribution of the patients throughout the State. These patients represent those discovered merely by routine examination of biopsy material at the State Health Laboratory, or the review of pathological material in one metropolitan hospital. Almost certainly the disease is not uncommon, and many cases may not be encountered by a medical man, while others are probably misdiagnosed, either with or without biopsy. We have found that clinicians almost without exception are unaware of the condition, although when questioned many recall having seen suspicious cases. There is evidence that the disease has a wide distribution throughout the world, and it is most improbable that it is confined in Australia to Queensland.

Differential Diagnosis.

Until such time as an antigen for skin testing is readily available, the diagnosis will probably remain a histological one. The histological picture is characteristic and striking, but it does closely resemble that seen in tularæmia and *lymphopathia venereum*.

Tularæmia is unknown in Australia and can readily be excluded by agglutination tests of the patient's serum with *Pasteurella tularensis*.

Lymphopathia venereum is also extremely rare in this country, and can be excluded in most cases by the clinical history or by means of the Frei test.

Reports of Cases.

CASE I.—L.W., a schoolboy, aged fourteen years, from Brisbane, was deeply scratched and bitten on the right hand by a cat which had been wandering wild in the neighbourhood. The boy was bitten "towards the end of December, 1950". The wound on his hand healed over, but remained raised and red for fourteen days. On January 21, 1951, the patient first became sick and feverish, and he was intermittently febrile from that time until he was subsequently admitted to hospital. On January 28 a lump was first noticed in the right axilla, and this was followed some days later by soreness in the same area. On February 14 the patient became nauseated and anorexic, and fever was apparent. The swelling in the axilla commenced to increase in size and was slightly fluctuant. Medical attention was first sought at this time, and penicillin was administered for four days without any improvement, the mass slowly increasing in size and becoming more painful. The boy remained feverish and obviously ill. The swelling in the right axilla became so pronounced that the attending doctor "suspected a sarcoma" and the patient was admitted to hospital. On March 6 an operation was performed and the mass in the axilla was removed completely. On the day after the operation the temperature was 104° F., the pulse rate was 125 per minute and respirations numbered 35 per minute; the axillary wound was clean and tender. The patient remained febrile (temperature up to 100° F.) for about one week, and there was a slight serous discharge from the wound, which, however, soon disappeared. He was kept under observation for some days, but his recovery was uneventful and he has remained in good health since.

Whilst he was in hospital numerous investigations were carried out. An X-ray examination of the chest, blood counts, and also several examinations of the sputum and urine revealed no abnormality. The Wassermann and Kline tests gave no reaction and the serum failed to agglutinate *Pasteurella tularensis*.

Blood and urine were collected and submitted to the Queensland Institute of Medical Research for virological investigation. The blood was inoculated into infant mice by intraperitoneal injection, also into weaned mice by intraperitoneal and intracerebral injection, and also into guinea-pigs. The urine was inoculated into guinea-pigs and adult mice. No virus was recovered.

An attempt was made to secure the cat which had scratched the patient, but as it was not available a litter mate was examined. The organs of the cat were inoculated into infant and weaned mice by various routes (intracerebral, intraperitoneal and intranasal), but no virus was isolated, nor was there any significant pathological change in the tissues. A smear was made from the teeth of the cat, close to the gum margin, and this revealed a large number and variety of organisms.

The tissue from the axilla was submitted to one of us (J.I.T.) for histological examination, and unfortunately, since the true nature of the lesion was not suspected, the whole specimen was fixed in formalin.

The specimen was roughly ovoid and measured 4·0 by 3·0 by 2·5 centimetres. A creamy substance exuded from the cut surface. There was also a mass of fat in which were several glands, the largest of which measured 2·5 by 1·5 by 1·5 centimetres. On microscopic examination an unusual granulomatous inflammation was found. The tissue was studded with small round and stellate abscesses, their centres being packed with polymorphonuclear leucocytes and with a palisading of epithelioid cells at the periphery. The size of these abscesses varied, and in some areas only scanty polymorphonuclear cells were present, the epithelioid reaction was prominent and occasional giant cells were present at the periphery. There was no true caseation. Much of the normal gland architecture was destroyed by these abscesses, but in the unaffected areas the sinuses were well preserved and the follicles in places hyperplastic. There was no evidence of any neoplasm, and no acid-fast bacilli or other organisms were found after an exhaustive search.

Late in 1952 a limited supply of antigen for intradermal tests was made available by courtesy of Colonel Bensted, of the Central Public Health Laboratory, London, and on November 3, 1952, almost two years after this patient became infected, an intradermal test with the "cat-scratch" antigen was carried out with a positive result. It was pleasing to be able to confirm our diagnosis, made previously on histological grounds.

CASE II.—J.R.T., a female subject, aged thirty-four years, from Cairns, north Queensland, noticed a tender mobile lump on the anterior surface of the left biceps for about two weeks. The mass was about one centimetre in diameter and firm to the touch. There was also a tender lump in the left axilla. The mass on the anterior surface of the biceps did not appear inflammatory and was apparently unaffected by sulphadiazine and penicillin therapy. The mass from the arm was excised under local anæsthesia and was found to be situated under the fascia about the middle of the left biceps muscle, and was richly supplied with blood vessels. The tissue immediately surrounding the mass was said to be necrotic and friable. This tissue was submitted to us for pathological examination. As a result of our examination a request was made for the axillary gland to be excised and submitted unfixed for culture and virological investigation. Portion of this axillary gland was to be examined histologically also. Two weeks later the axillary gland was submitted. The patient made an uneventful recovery. No history of either a scratch or bite from a cat was obtained.

The tissue from the anterior surface of the biceps was a small lymph gland which presented the granulomatous reaction we associate with this form of lymphadenitis. In places the epithelioid reaction was predominant, but in other areas there were abscesses, some of which were stellate in shape. The inflammatory reaction was infiltrating the neighbouring connective tissue planes, a feature quite unlike the behaviour of tuberculosis. No acid-fast bacilli or other organisms were found in the sections.

Portion of the axillary mass was kept for histological examination, and this revealed a lymph gland containing the same rounded and irregular areas of necrosis. These areas had a narrow epithelioid margin, within which were eosinophilic zones of necrosis. Occasional scattered and degenerate polymorphonuclear cells were present in the centre of some necrotic areas, but these were not a conspicuous feature as in the previous biopsy. There was no true caseation, and no giant cells or acid-fast bacilli were found. The histological picture was characteristic of that seen in the later stages of this form of adenitis.

The unfixed axillary gland was submitted to the Queensland Institute of Medical Research for investigation. Portion of the gland was injected into the amniotic, chorio-allantoic and yolk sac cavities of eggs, and these inoculations were carried on for five, three and three passages respectively without any virus being recovered.

Bacteriological and mycological cultures, also impression smears stained by the Giemsa technique, failed to reveal any organism.

Some of the tissue was inoculated into suckling mice and into weaned mice by the intraperitoneal, intracerebral, subcutaneous, intranasal and intradermal routes. Two kittens were inoculated intraperitoneally, and guinea-pigs by the intraperitoneal, intracerebral and subcutaneous routes. No virus was recovered.

Serum from the patient failed to agglutinate *Pasteurella tularensis*.

CASE III.—J.C., a boy, aged seven years, was admitted to the Mackay hospital on January 31, 1951, for investigation. He gave a history that eighteen months previously he had developed slight lumps on the left side of his neck, which had remained about the same size. One week prior to his admission to hospital another lump had developed beneath the angle of the mandible on the right side, and this had rapidly and greatly increased in size. On examination the left jugular and right submandibular glands were found to be enlarged and some carious teeth were present. The liver and spleen were not enlarged, but there was slight enlargement of the axillary and inguinal glands. The lung fields were clear, and there was no mediastinal enlargement. The Mantoux test gave a positive reaction, and no significant abnormality was present in the blood picture.

A lymph gland from the left side of the neck was taken for biopsy on February 6, 1951, and submitted to one of us (J.I.T.) for examination. The incision healed cleanly, but two days later the child commenced to have an evening rise of temperature up to 99·8° F., and the mass of glands in the right submandibular area began to enlarge. On February 15 sulphadiazine and penicillin therapy was commenced without effect, and two days later a carious stump was extracted from the right lower jaw. On February 20 the mass in the left posterior triangle increased in size and it was noted to be fluctuant in the centre, and six days later a pointing abscess was incised and a portion of the suppurating gland together with some of the pus was submitted for examination. The child made an uneventful recovery, although four months later a few slightly enlarged glands were still detectable.

The first biopsy revealed the characteristic granulomatous reaction comprising stellate abscesses with epithelioid cell palisading at the periphery. In the second biopsy there were irregular areas of necrosis with a margin composed of

epithelioid cells. Groups of degenerating polymorphonuclear cells were scattered in the necrotic areas. In other areas of the gland plasma cell infiltration was a prominent feature. No acid-fast bacilli or other organisms were found in the sections.

Serum from the patient failed to agglutinate *Brucella abortus, Pasteurella tularensis, Proteus* OX19, *Proteus* OXK or *Coxiella burneti*. Agglutination tests with five strains of leptospirae were also negative.

The pus and unfixed gland tissue were submitted to the Queensland Institute of Medical Research for investigation. The pus was mucoid, sticky, greyish and blood-stained. It was inoculated into suckling mice, into adult mice by the intracerebral, intranasal, subcutaneous and intraperitoneal routes, and also into two guinea-pigs. Even after many passages no virus was recovered. Impression smears failed to reveal any organisms, and no growth was obtained in either bacteriological or mycological cultures. Two passages were carried out in the chorio-allantois and the yolk sac of eggs without recovery of any virus. The gland, consisting of soft irregular fragments, was inoculated into suckling mice, adult mice and guinea-pigs as well as the chorio-allantois and yolk sac of eggs, but again no virus was recovered.

A few beaded fusiform organisms were grown on culture, but their true nature could not be determined.

CASE IV.—C.H.C., a male subject, aged twenty-six years, of Brisbane, developed a swelling of the lymph glands in the inguinal region on one side. The swelling increased for a week, during which time an attempt was made to aspirate them without success. The glands were then excised and some pus was detected during their removal. The wound healed without delay. The patient was not febrile at any stage, and no other enlarged glands were detected. He has remained well and free of symptoms since the removal of the glands.

The patient had recently acquired a cat and was handling it more than usual one week before the swelling in the groin occurred. There is no definite history of his having been scratched by the cat.

The diagnosis was originally made histologically, but some months later this was confirmed by a positive reaction to the intradermal test with the "cat-scratch" antigen.

CASE V.—Mrs. F., aged fifty-one years, of Brisbane, owned a kitten which three months previously had been very ill for two weeks. It recovered spontaneously. The patient was frequently scratched on the hands and mainly on the right side. She first complained of soreness in the right axilla of ten days' duration. Swelling and soreness also occurred in the right groin three days later. After five days the swelling and soreness in the groin disappeared, but the axilla remained tender. On examination a small tender gland was palpated in the right axilla. No biopsy was obtained unfortunately, but the patient gave a positive reaction to the intradermal test with the "cat-scratch" antigen. Recovery was uneventful.

CASE VI.—M.I.M., a married woman, aged thirty years, the wife of a farmer at Yeppoon, central Queensland coast, developed an enlargement, 2·5 centimetres in diameter, of the axillary lymph glands on one side. The swelling was firm, mobile and tender to such a degree that the arm could be moved only slightly. Sulphadiazine and penicillin therapy produced no improvement. The mass was excised and a histological examination was made. The diagnosis of reticulosis was made from the biopsy and deep X-ray therapy was given to the axilla. Subsequent to this the evidence of inflammation subsided except for slight glandular enlargement. The true nature of the lesion was recognized after review of the sections, before the patient left hospital. A Frei test was performed, but produced no reaction.

CASE VII.—A.N., a boy, aged six years, from Boonah, southern Queensland, presented with a history of having a lump on the side of the neck, which appeared to be growing larger. On examination he was found to have a hard mobile gland in the right posterior triangle, which was about two centimetres in diameter. The lymph glands elsewhere were slightly enlarged and "shotty". The cervical gland was removed and a diagnosis of reticulosis was made. A full blood count revealed no abnormality, and an X-ray examination of the chest revealed no lesion in the lungs or mediastinum. He received a course of deep X-ray therapy. The correct diagnosis was made at a later review of the biopsy sections. The child has remained well since. There was a history of contact with cats, but not of a scratch by a cat.

CASE VIII.—A.J.C. was a boy, aged five and a half years, also from Boonah. The boy's mother first noticed a small gland on the left side of the neck, which became enlarged during the next two or three weeks, to attain a diameter of one centimetre. No sore throat, but slight fever was present. On examination of the patient a small, hard, mobile gland was palpable in the left posterior triangle about 1·5 centimetres in diameter. There were enlarged glands of lesser size in both axillæ. The spleen was not palpable, but the tonsils were moderately enlarged. The hæmoglobin value was 12 grammes *per centum* and the white cell count was normal.

A gland was removed for biopsy and was reported on as showing acute infective suppurative lymphadenitis. The true nature of the condition was recognized on later review. After the biopsy a few more lymph glands became enlarged, but since then the child had remained well. There was a history of contact with cats, but not of any scratches by a cat.

CASE IX.—R.E., a boy, aged eight and a half years, developed enlarged lymph glands in the right epitrochlear and right axillary areas, accompanied at first by fever. The enlarged glands were painful and tender. A gland was removed for biopsy. At operation the glands were adherent, and one gland ruptured during removal, with escape of thick yellow material. A full blood count revealed no abnormality. A Mantoux test produced a negative result, and the Paul-Bunnell test produced no reaction. X-ray examination of the chest revealed no abnormality. The diagnosis was made from the biopsy.

CASE X.—E.W.G., aged fifty-eight years, a farmer from Esk in southern Queensland, presented with a very painful gland in the right groin, with which was associated a small hernia. He was otherwise symptomless and afebrile. There was a small lesion resembling psoriasis, of doubtful duration, on the right leg, 7·5 centimetres above the ankle. The gland was removed and the diagnosis was made from the biopsy. There was a history of contact with horses, pigs and cattle, but not with cats. Recovery was complete and uneventful. He is said to have had numerous splinters of wood in his hands.

CASE XI.—S.W.H., a male, aged twenty-six years, from Innisfail in north Queensland, developed enlarged glands on the right side of the neck. These had been present for about four weeks and were steadily increasing in size. The patient was otherwise symptomless, and the blood picture revealed no abnormality. The glands were removed and the diagnosis was made histologically. Recovery was complete and there has been no recurrence of the glandular enlargement since.

CASE XII.—J.M., a boy, aged eleven years, from Mareeba in north Queensland, had a swelling in the submental region of several months' duration. This mass increased in size, but was painless, and there was no apparent inflammation. Clinically the lesion was thought to be a thyroglossal cyst. The biopsy consisted of a mass of tissue measuring 2·3 by 1·2 by 0·7 centimetres, and the histological picture was that of the characteristic suppurative lymphadenitis. Recovery was complete.

CASE XIII.—E.F., a married woman, aged forty-eight years, from Herberton in north Queensland, developed two enlarged lymphatic glands in the right axilla. These glands increased in size over a period of one month, and there seemed no adequate explanation for the enlargement. The patient was otherwise symptomless. The diagnosis was made from the biopsy and there has been no recurrence. It was not possible to obtain details of contact with animals.

CASE XIV.—B.T.B., a male subject, aged thirty-six years, from Gympie, southern Queensland, developed an enlarged epitrochlear gland without obvious cause. The gland steadily increased in size over a period of four weeks. The gland was removed and the diagnosis was made from the biopsy. No follow-up was possible.

CASE XV.—E.K., a female, aged forty-seven years, from Mount Isa in north-western Queensland, developed what appeared to be an abscess of the left epitrochlear gland. The biopsy consisted of a mass of fibro-fatty tissue, in which was embedded a gland 1·2 centimetres in diameter. The diagnosis was made histologically. No follow-up was possible.

CASE XVI.—E.F., a male subject, aged forty years, from Mount Isa, developed an enlarged lymph gland in the inguinal region for no apparent reason. Several small glands were submitted embedded in a mass of fat. One gland was dark, with scattered necrotic areas. The histological picture was characteristic, and numerous small stellate abscesses were conspicuous. Recovery was apparently complete after the biopsy.

Discussion.

It is apparent that there occurs in Queensland, and almost certainly elsewhere in Australia, a regional non-bacterial suppurative lymphadenitis presenting an unusual histo-

logical appearance. There is some evidence to suggest that the disease is viral in origin. There is much evidence to suggest that there is an association between this disease and contact with cats. Some authors (Mollaret, 1950; Fox, 1952) state that the disease may also be transmitted by injury to the skin by other agents, such as thorns, wood splinters, mosquitoes or pieces of bone. In several published series of cases (Debré *et alii*, 1950; Daniels and MacMurray, 1951) the association with cats was more than coincidental.

There appears to be an immunity of the cats to the infecting agent, and this suggests that they may act purely as passive carriers, the source of the infection being one of the small birds or rodents on which they prey.

There is some evidence in our series to suggest that there may be a seasonal incidence, since the vast majority of our patients have come under observation in the summer and early autumn. The significance, if any, of this observation is as yet unknown.

Our impression is that in the majority of cases the disease will follow a benign course and recovery will occur without sequelæ. Of the three cases previously described by us in which lesions of this type were present, one patient died with an associated encephalitis; if, as seems highly likely, the ætiological agent was the same in these three cases, one cannot regard the condition as being necessarily benign or localized in character. Considerable support is lent to this view by a recent report of a case of encephalitis associated with cat-scratch fever in the United States of America (Stevens, 1952).

The main purpose of this report is to draw the attention of medical practitioners and pathologists to this condition, so that every opportunity may be afforded to investigate both the ætiology and the epidemiology of the disease.

Summary.

A curious regional non-bacterial suppurative lymphadenitis has been described in 16 cases in Queensland. It is considered that this condition is identical with the disease described as "cat-scratch fever" in America, France and England.

Patients presenting with the lymphadenitis often but not invariably give a history of contact with cats. The disease is thought to be caused by a virus.

The clinical features and pathology of the disease are discussed. The affected glands present a characteristic histological picture.

The lymphadenitis is not noticeably affected by sulphonamide or penicillin therapy, but in most cases the disease follows a benign course and recovery occurs without sequelæ. However, there is evidence to suggest that the condition may not necessarily be always benign or localized in character.

Acknowledgements.

We acknowledge gratefully the assistance of those medical practitioners who cooperated by submitting material. Our thanks are due to the technical staff of the Queensland Institute of Medical Research for their aid in the laboratory investigations. Dr. W. L. Jellison, of the Rocky Mountain Laboratory, Montana, kindly supplied the *Pasteurella tularensis* antigen. Especial thanks are due to Colonel H. J. Bensted, of the Central Public Health Laboratory, Colindale, for supplying the "cat-scratch" antigen.

The photomicrographs were prepared by the late Mr. G. E. Thomson, of the University of Queensland Medical School.

References.

BENSTED, H. J. (1952), "Cat-scratch Fever", *Lancet*, 1: 1067.

CAMPBELL, E. S. K., and WHEATON, C. E. W. (1952), "Cat-scratch Fever", *Lancet*, 1: 975.

DANIELS, W. B., and MACMURRAY, F. B. (1951), "Cat-scratch Disease", *Arch. Int. Med.*, 88: 736.

DEBRÉ, R., LAMY, M., JAMMET, M. L., COSTIL, L., and MOZZICONACCI, P. (1950), *"La maladie des griffes du chat"*, *Bull. et mém. Soc. méd. Hôp. Paris*, 66: 76.

FOX, R. A. (1952), "So-called Cat-scratch Fever", *Arch. Path.*, 54: 75.

GARAI, O. F. (1952), "Cat-scratch Fever. A Case in England", *Lancet*, 1: 646.

INGLIS, J. A., and TONGE, J. I. (1950), "A Disease with Visceral Granulomatous Lesions of Unknown Ætiology", *M. J. Australia*, 1: 433.

MOLLARET, P., REILLY, J., BASTIN, R., and TOURNIER, P. (1950). *"Sur une adénopathie régionale subaiguë et spontanément curable, avec intradermo-réaction et lésion ganglionnaires particulières"*, *Bull. et mém. Soc. méd. Hôp. Paris*, 66: 424.

MOLLARET, P., REILLY, J., BASTIN, R., and TOURNIER, P. (1950), *"Documentation nouvelle sur l'adénopathie régionale subaiguë et spontanément curable décrite en* 1950; *la lymphoréticulose bénigne d'inoculation"*, *Presse méd.*, 58: 1353.

MOLLARET, P., REILLY, J., BASTIN, R., and TOURNIER, P. (1950), *"Une maladie ganglionnaire nouvelle: adénopathie régionale subaiguë spontanément curable avec intradermo-réaction et lésions histologiques particulières"*, *Presse méd.*, 58: 282.

MOLLARET, P., REILLY, J., BASTIN, R., and TOURNIER, P. (1951), *"La découverte du virus de la lymphoréticulose bénigne d'inoculation"*, *Presse méd.*, 59: 681, 701.

STEVENS, H. (1952), "Cat-scratch Fever Encephalitis", *Am. J. Dis. Child.*, 84: 218.

Legends to Illustrations.

FIGURE I.—Accumulation of epithelioid cells, not yet showing necrosis (× 105).

FIGURE II.—Early necrosis is now evident at the centre of the epithelioid cell accumulation (× 105).

FIGURE III.—Polymorphonuclear leucocytes have now invaded the necrotic centre (× 105).

FIGURE IV.—Well-developed round and irregular abscesses are seen (× 105).

FIGURE V.—Well-developed round and irregular abscesses are seen (× 105).

FIGURE VI.—Epithelioid cell margin at higher magnification (× 450).

CEREBRAL ASTROCYTIC GLIOMATA, WITH THE REPORT OF A CASE.

By IRVINE J. HUNTER,

Reginald Maney Lake Research Scholar and Amy Laura Bonamy Scholar.

(From the New South Wales Mental Hospitals Laboratory, Department of Pathology, University of Sydney.)

SCHERER (1935*a*) was the first to stress the need for a change of attitude towards the gliomata and a change of approach to research in this field, pointing out the limitations of diagnosis by "cell type" (1935*b*). The movement has been begun by him with his method of "complete" examination of these tumours; but as yet it does not seem to have had very wide repercussions, at least in practice.

In former times encephalic tumours were classified simply according to their degree of hardness. To Virchow we owe the recognition of the glial origin of the majority of these tumours and the term "glioma" (Courville, 1950). He distinguished hard and soft varieties of "glioma", and also "sarcoma". The term "gliosarcoma" was introduced by Borst (Scherer, 1940*b*).

As Adami and Nicholls (1911) and Ewing (1940) have recognized, there is no fundamental error or contradiction involved in the term "gliosarcoma". Sarcomata are malignant tumours of connective tissue cells, just as carcinomata are malignant tumours of epithelial cells. The purely doctrinal concept of rigid germinal layers formerly dominated embryology, and still dominates thinking in pathology. The three cellular layers of the early embryo are merely an incident of development—a convenient ordering of the cellular units as a stage in morphogenesis. Typical epithelia can be formed by the mesoderm, as is shown in the uterus and kidney, and a typical, although specialized, connective tissue is formed by the ectoderm in the astroglia and oligodendroglia of the central nervous system.

Similarly, the tumours of glial tissue, although having distinctive features of their own, have features in common with neoplasms of the other connective tissues,[1] and very

[1] For instance, the prominent vascular proliferation seen in anaplastic gliomata, although unusual in type, is reminiscent of the prominence of blood vessels often found in sarcomata.

naturally Virchow designated the anaplastic tumours, purely descriptively, as sarcoma. However, any revival of the term "gliosarcoma" would probably tend towards confusion, because, firstly, the sarcomata are characterized by blood-stream metastasis, which is not a characteristic of the glial tumours, and, secondly, the slow-growing, histologically well-differentiated astrocytic gliomata of the cerebrum, such as the one reported in this paper, have an infiltrative type of growth and thus should also be regarded pathologically as malignant.

The term "cerebral" should be used in its correct sense of "pertaining to the cerebrum", which is not the whole brain but that part of it rostral to the isthmus—in other words the midbrain and forebrain. The adjective pertaining to the brain as a whole should be "encephalic", and this includes "cerebral", as well as "pontine", "medullary" and "cerebellar".

Combined macroscopic and microscopic research on glial tumours was begun by Virchow, and in the early years of this century the most important facts known to us today about the chief types of glioma had already been discovered (Scherer, 1940*b*). In that paper Scherer has given an excellent historical account, with some very pertinent comments, of the development of ideas upon and the approach to the gliomata. He pointed out that things began to take a wrong turning with a paper by Ribbert in 1918; this paper opened the period of glioma research characterized by the arbitrary emphasis laid on merely cytological studies, with the almost complete neglect of the numerous other aspects of glioma pathology, the dominating method now becoming the cytological study of a fragment of glioma tissue with the implicit supposition that it is representative of the whole tumour. This attitude found its most dogmatic expression in the well-known monograph of Bailey and Cushing (1926).

Scherer in the same paper enumerated the achievements of this "histogenetic" period as being the definition of the medulloblastoma and the cerebellar astrocytoma (both independently of the histogenetic principle), and the description of the oligodendroglioma (which, however, includes tumours of different behaviour and is probably not a morbid entity). For the rest it has been an elaboration of systems of classification, an endeavour to fit facts into preformed patterns, and the forgetting of many important facts which were known in former times.

There are two points of view from which the histogenetic classifications can be attacked. Firstly, in regard to the tumours less well differentiated histologically, there is the idea embodied in such terms as "spongioblastoma", "astroblastoma" *et cetera* that the cells are not fully differentiated embryologically. This view has been criticized by various authors, and there has been a tendency away from it, with an increasing realization that such appearances are usually the result of anaplasia. Secondly, there is the whole basis and method of approach, which concentrates attention solely on the histological appearance of the tumour tissue. This has been attacked by Scherer, who has instituted studies of gliomata by his "complete" method of examination (1935*a*, 1940*b*).

Glioma cells have been grown in tissue culture (for example, Russell and Bland, 1933 and 1934; Cox and Cranage, 1937). The most important result has been that of Russell and Bland (1934) that cultures in two cases of so-called "polar spongioblastoma" gave rise to ordinary astrocytes. They concluded that the polarity of the cells in most cases was caused by the direction of the fibre tracts, but Scherer (1940*a*) regarded this piloid type of astrocytoma as having distinctive biological characteristics.

This question of architecture proper to gliomata and that depending upon the preexisting architecture of the brain was dealt with by Scherer (1938). Cox (1933) emphasized that account must be taken of cells of the invaded nervous tissue included in the tumour.

That different histological appearances could be found in different parts of one glioma was recognized by Virchow (Scherer, 1940*b*). This fact of diversity in a single tumour was admitted by Bailey and Cushing (1926), but throughout the histogenetic period has been largely ignored, and attempts have been made to classify tumours according to the "predominant" cell type. The presence of variation in structure, with a failure to recognize its common occurrence, has led to subdivisions of tumour types. This variation in one and the same tumour was emphasized by, for example, Munro, Edwards and W. Russell (1941) and by Willis (1948).

In Bailey and Cushing's original monograph (1926) there were listed sixteen different types of tumour, including *astrocytoma protoplasmaticum*, *astrocytoma fibrillare*, astroblastoma, *spongioblastoma unipolare* and *spongioblastoma multiforme*.

Bailey (1933) did not divide astrocytomata, adopted the name "*glioblastoma multiforme*" instead of "*spongioblastoma multiforme*", and replaced "*spongioblastoma unipolare*" by "*spongioblastoma (polare)*". He maintained this classification in the second edition of his book (Bailey, 1948).

Other terminology has been used by other authors, often using somewhat different criteria, sometimes purely cytological, often partly histological. A comparative list of some of these terms was given by Wilson (1940) in his text-book.

Bailey himself (1933, 1948) admitted that the "astroblastoma" is poorly defined, and the tendency has been to drop this grouping. As was mentioned above, the "spongioblastoma", as defined by Bailey, has been shown by Russell and Bland (1934) to be probably a type of astrocytoma, although these authors state that rarely there occur true tumours of spongioblasts, which are rapidly growing and highly invasive. Such cases were described by Cairns and Russell (1931) and by Russell and Bland (1933); in the latter case culture gave rise to cells resembling spongioblasts.

This leaves of the tumours mentioned above astrocytoma and "*glioblastoma multiforme*" as clearly defined histological types, within both of which structural variation may occur.

Carmichael (1928) suggested a rather similar classification into "astroblastic" and "spongioblastic" tumours.

That a protoplasmic type of astrocytoma may give rise to "*glioblastoma multiforme*" was admitted by Bailey and Cushing (1926). The presence of nodules of "sarcoma" in otherwise typical "glioma" tumours had, however, been discovered by Stroebe more than thirty years before this time (Scherer, 1940*b*).

That "*glioblastoma multiforme*" is an anaplastic type of astrocytic tumour has now received fairly wide recognition. Willis (1948) suggested the name "astrocytic glioma" to cover all this group, and does not favour clear-cut subdivisions, pointing out that although some are more anaplastic than others there is considerable diversity and interrelation of histological structure in the group. Thus on the basis of histological structure alone subdivision into well-defined entities is not possible.

Kernohan, Mabon, Svien and Adson (1949) have endeavoured to introduce Broders's classification into glioma terminology. All types of tumour are regarded as lending themselves to division into four grades. The application of this doctrine in detail to the astrocytic group, including "*glioblastoma multiforme*", is given by Svien, Mabon, Kernohan and Adson (1949). A somewhat similar system of grading has been suggested by Ringertz (1950).

There are strong reasons for rejecting such a system. The chief objections to it are as follows:

1. Although it is based on the total histological picture and not on merely the character of the cells, it perpetuates the method of classification of the gliomata by structure alone and ignores other important facts about the tumour (see below).

2. It is based on the fallacy, or at least tends to encourage it, that examination of small pieces of a tumour is adequate. This is certainly not so in the gliomata

because of the great structural diversity found in the one tumour, a point that has been emphasized by, among others, Munro, Edwards and W. Russell (1941), and by Willis (1948).

3. It gives rise to a false sense of exactitude.

4. As far as tumours in general are concerned, examples are met with that, while histologically apparently benign, are none the less malignant, as is shown by their giving rise to metastases. (This is briefly discussed by Willis, 1948, at page 19.)

No doubt statistics would prove the merits of Broders's classification, and such a grading might be useful provided that it was based on examination of adequate portions of the tumour and that its use was confined to the graphs of the statistician. It is well known that by and large more anaplastic tumours are more malignant in their behaviour, and the larger the series of cases the more the errors and inconsistencies in particular cases are hidden; but the accumulation of imposing figures does not make the classification any more likely to be right in any individual case, and it is to individual cases that it has to be applied in practice.

How then can the gliomata be classified? Scherer (1940*b*) has pointed out that our knowledge of the gliomata can be advanced only by a return to the combined macroscopic and microscopic approach used before the paper by Ribbert (1918) was published, together with a consideration of their natural history. In this way morbid entities may be defined instead of microscopic pictures. It has been seen above that Willis (1948), on the basis of histological structure, thought that no clear-cut divisions could be drawn in the group of astrocytic gliomata.

Scherer emphasized two points. Firstly, for purposes of research only necropsy material can provide an adequate opportunity of investigation, and secondly, the method of examination must be much more extensive than has usually been the case in the past.

A certain distance has already been covered, and it appears that, among other factors, the site in the brain will enter into the classification.

The circumscribed, cystic astrocytic tumours of the cerebellum which occur in children were defined as a morbid entity by Cushing (1931). They are quite different from the histologically often identical astrocytomata of the cerebrum. The latter show a highly infiltrative, or diffuse, type of growth, and, according to Scherer (1940*c*), a circumscribed astrocytoma of the cerebrum has never been satisfactorily demonstrated. Nevertheless the two are still classified together on the basis only of cytological resemblance (for example, Bailey, 1948).

As was stated above, areas of *"glioblastoma multiforme"* may be found in astrocytoma of the cerebrum. Grinker and Bucy (1949) stated that some astrocytomata, particularly the protoplasmic type, occasionally undergo "malignant transformation", and the prevailing impression would seem to be that while protoplasmic astrocytomata are perhaps suspect, "glioblastoma" developing in a fibrillary astrocytoma is rare. However, Scherer (1940*c*) has presented evidence that if the growths are examined adequately, such anaplastic areas can be found in the majority of cases.

One of the most concise, useful and practical articles on the gliomata is "The Forms of Growth in Gliomas and Their Practical Significance" (Scherer, 1940*a*).

The following is a case of cerebral fibrillary astrocytoma, obviously of considerable standing, with the supervention of anaplastic "glioblastomatous" growth which caused death by interference with the circulation of the cerebrospinal fluid. Scherer (1940*c*) has studied these new growths and has described the main features which enable them to be defined as a morbid entity. The following case conforms in almost every detail to Scherer's description, and is presented to bring to notice the characters of this type of growth and also to emphasize that *"glioblastoma multiforme"* may arise from a slowly growing, well-differentiated fibrillary astrocytoma.

The manner in which the case report is set out is based upon that recommended by Scherer.

Method of Examination.

Adequate study requires many large celloidin sections including the whole glioma and surrounding tissue, or else (as in the present case) many paraffin sections from various parts of the tumour and surrounding tissues. If this latter method is used, a drawing (Figure II) should be made, to indicate clearly the relation of the paraffin blocks to the tumour mass. Scherer's "complete" method of examination with large celloidin sections allows a more thorough investigation, and is preferable for systematic studies. In either case a few blocks are cut by frozen section for metallic impregnations, but these are regarded as merely adjuvant and not as the sole criterion of the nature of the tumour.

Length of history, site, macroscopic features, mode of spread, degenerative changes *et cetera* are all considered in addition to the histological appearance of the tumour tissue in characterizing the tumour type.

Report of a Case.

The subject was a male, aged sixty-five years (case number N.P.87).

Duration of Symptoms.

The duration of symptoms was unknown. The patient died about two weeks after his admission to a mental hospital. No operation for the tumour had been performed. While he was in hospital the patient was stuporose. There were present spasticity, more pronounced on the left; a left-sided Babinski response and intermittent Parkinsonian tremor of the left upper limb; several convulsive seizures occurred, which were predominantly left-sided.

Weight of the Brain after Fixation.

The weight of the brain after fixation was about 1405 grammes. The right half of the forebrain weighed about 575 grammes, the left half of the forebrain about 690 grammes.

Macroscopic Findings in the Brain.

On macroscopic examination of the brain, the arteries at the base of the brain were not affected by atheroma, and the piaarachnoid over the whole surface of the brain appeared normal. Part of the *falx cerebri* was attached to the specimen, and this also was normal.

Examination of the hindbrain and fourth ventricle revealed no abnormality.

The midbrain could not be examined properly because the brain had been fixed with this structure in acute anteflexion, so that the hindbrain rested on the frontal lobes; but no obvious abnormality could be seen, and the cerebral aqueduct was not dilated.

There was no dilatation of the cavity of the third ventricle, and as far as could be ascertained there was no grossly visible abnormality of the structures of the interpeduncular fossa.

There was a smooth projection of the medial part of the left thalamus, which extended about one centimetre across the mid-line and had caused deformation of the right thalamus, and evidently obstruction of the right interventricular foramen, as on cutting into the hemisphere the right lateral ventricle was found to be dilated, especially at the region of junction of the central part with the posterior and inferior horns (Figure I). The white matter of this hemisphere was considerably congested, but the grey matter of both cortex and basal nuclei looked normal.

The left interventricular foramen was normal and the lateral ventricle was not dilated. However, there was almost complete loss of the internal architecture of the left cerebral hemisphere, and an apparently neoplastic mass projected medially from the area of the thalamus. This mass and the neighbouring internal capsule were firm in consistency. In contrast to this, a very large part of the interior of the hemisphere was much softer than normal. Much of the softened area had a moth-eaten, lacunar appearance (Figure I).

This softened area involved the cortex in three places. In front of and below the genu of the *corpus callosum* was a region of cortex which was softer than normal and projected across the mid-line, indenting the *gyrus rectus* and medial frontal gyrus of the opposite side. A more extensive softened area of cortex was situated to the medial side of the left temporal pole, involving the uncus, and softish tissue of

whitish colour was to be seen in the region of the stem of the lateral sulcus and the orbital surface of the frontal lobe. The third apparent area of cortical involvement was in the region of the posterior ramus of the lateral sulcus, where a partial obliteration of the sulcus seemed to have occurred.

The unsoftened part of the hemisphere was congested, particularly in its dorsal portion.

There were irregular, low, subependymal elevations to be seen on the wall of both lateral ventricles.

Localization and Extent of the Tumour.

The main portion of the tumour occupied the major parts of the frontal, parietal and temporal lobes on the left side. The olfactory tract was involved. The microscopic limit of the tumour was 1·5 centimetres or more in excess of the macroscopic limit of the softened area.

The firm tumour mass of the thalamus measured about 2·5 by 3·0 centimetres in horizontal section and was localized to this region.

The tumour had extended into the tegmentum of the midbrain.

Sections from the opposite thalamus and central white matter did not show definite evidence of invasion by the tumour.

Cytology and Fibre Formation.

The bulk of the tumour was a typical fibrillary type of astrocytoma with a moderate amount of formation of glial fibres (Figure III).

The firmer mass occupying the thalamic region had the structure of a typical example of the anaplastic, pleomorphic type of astrocytic glioma—so-called "*glioblastoma multiforme*" (Figure V)—but there was a greater formation of glial fibres than is usual in this type of tumour. Many multinucleated giant cells were present, the nuclei usually having a peripheral arrangement. Multinucleated non-neoplastic astrocytes from the invaded tissue (as described by Cox, 1933) were also to be seen, but these were of quite different appearance, the nuclei being more regular and paler, and often having a distinct nucleolus, while the cytoplasm usually showed definite evidence of processes.

In the tegmental region the tumour showed some degree of anaplasia, but not to the same extent as in the thalamus. A number of neoplastic giant cells was to be seen.

Average Cellularity.

The average cellularity (0·01 square millimetre, thickness 20μ) in the anaplastic portion (thalamus) varied from about 212 to about 108, depending partly on the amount of œdema; and in the astrocytic portion from about 55 to about 12.

Mode of Growth.

The mode of growth was diffuse infiltration in both white and grey matter. Infiltration was present of the meninges of the orbital surface of the frontal lobe and in the posterior ramus of the lateral sulcus by fibrillary astrocytic cells (Figure IV).

Structure

The structure was almost completely amorphous, and there were few secondary structures. ("Secondary structures" are formed by the appearance of neoplastic cells in relation to preexistent structures such as vessels, nerve cell bodies or fibre bundles. They may be seen both in areas not diffusely invaded and in heavily invaded areas (see Scherer, 1938). Perivascular secondary structures were seen in the subcortical white matter of both frontal and occipital lobes (Figure VII), and early perineuronal secondary structures in the cortex in an area of temporal cortex near the posterior end of the tumour.

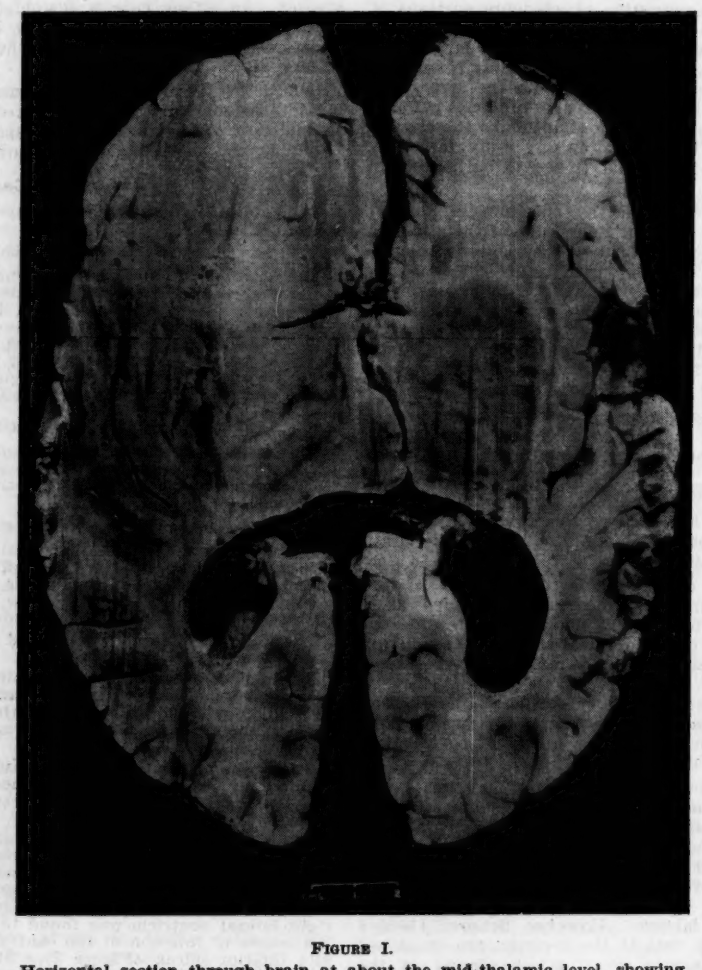

FIGURE I.

Horizontal section through brain at about the mid-thalamic level, showing the maximum extent of the tumour.

Preexistent Structures.

Both nerve cell bodies and myelinated fibres had been largely destroyed, in both the anaplastic and the astrocytomatous parts of the tumour. The structures that remained were in a state of degeneration. However, the internal capsule was well preserved.

Mesenchymal Stroma.

The vessels of the astrocytomatous portion were of normal appearance, but in the anaplastic portion typical thickened blood vessels were present, especially in the region bordering the third ventricle (Figure VI). Thickening of the endothelium and of the adventitial coat could be seen. In spite of some degree of anaplasia and the presence of neoplastic giant cells similar to those in the thalamic region, the vessels in the tegmental extension were of normal appearance.

Degenerative Changes.

The astrocytomatous part showed œdema and the formation of small cystic spaces. *Corpora amylacea* were very numerous in the involved olfactory tract and also in the subependymal region of the lateral wall of the posterior horn of the left lateral ventricle.

No necrosis was seen in the anaplastic part. There was some œdema, especially of the region bordering the third ventricle. Calcification (or ferugination) of vessels was a feature in the zone of transition between the astrocytomatous and anaplastic portions of the tumour.

Other Regions of Brain.

The subependymal elevations of the lateral ventricles appeared to be caused by proliferation of subependymal glia, and not to be neoplastic in nature.

The tectum of the midbrain, the pons, the *medulla oblongata* and the cerebellum were substantially normal. Sections stained for myelin showed no noticeable degeneration of fibre tracts in the *medulla oblongata* or in the upper part of the spinal cord.

Discussion.

This case shows well the features of the cerebral astrocytoma.

The most important feature of these tumours is that, with the possible exception of cases of piloid astrocytoma (so-called "polar spongioblastoma") occurring in the hemispheres, they are probably always widely infiltrative and never circumscribed; perhaps in all cases by the time symptoms appear they involve a large part of the hemisphere, and often the other hemisphere as well. They may spread across the mid-line, not only by the *corpus callosum*, but also by other routes such as the anterior commissure (Scherer, 1940*a*). The latter author was of the opinion that the balance of evidence favoured a primarily diffuse type of neoplastic growth rather than spread from an initially limited centre.

They thus contrast sharply with the cytologically identical tumours of the cerebellum, in which the zone of infiltration is usually narrow and complete surgical removal is possible. According to Scherer, a circumscribed astrocytoma of the cerebrum has never been satisfactorily demonstrated. Probably they are never susceptible of complete removal. Often these tumours are so slow-growing that the clinical results of operation may be eminently satisfactory. This, however, does not justify casting aside the principles of pathology and designating as benign a tumour whose most notable feature is the widespread infiltrative nature of its growth. The only type of gliomatous tumour whose growth is ever of a strictly expansive type and thus has the characteristics of benignity is the ependymoma (Scherer, 1940*a*).

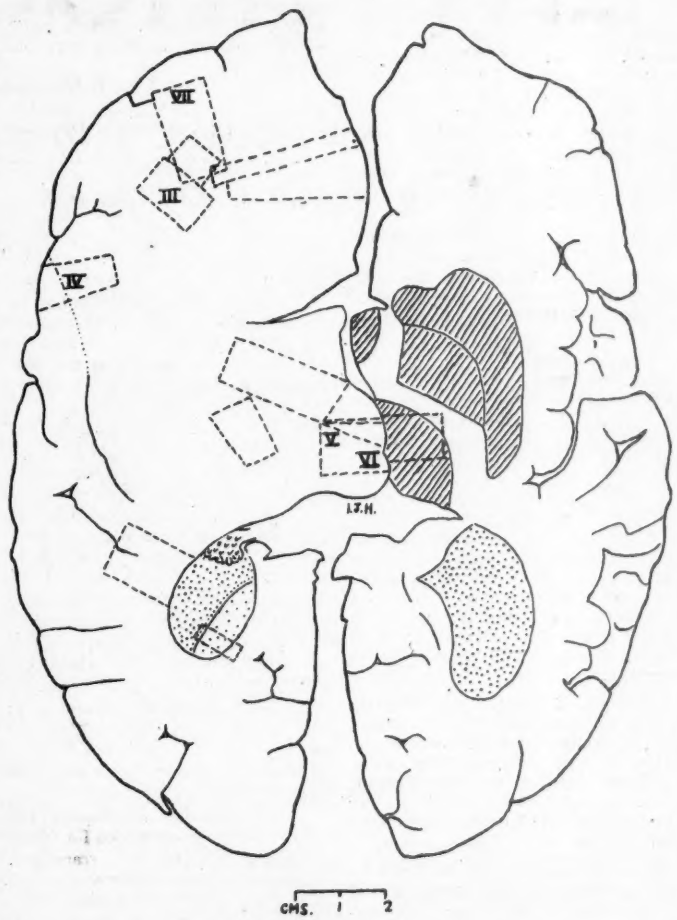

FIGURE II.

Drawing of the section shown in Figure I. The relative positions of some of the blocks examined microscopically are shown projected onto this plane, and the approximate locations of the fields shown in the photomicrographs are indicated by the numbers III to VII.

On macroscopic examination the cerebral astrocytomata have no definite edge; indeed, no tumour may be apparent at all, but just œdema of the central white matter. This is well illustrated by the present example. If such growths are apparent, it is usually because of degenerative change. This sometimes takes the form of a single large cyst, such as is characteristic of the cerebellar astrocytoma, but more often there are numerous small cystic spaces, a condition referred to by Scherer as "microcystic degeneration". This appearance can be seen in Figure I, the diameter of these cysts being from less than 0·5 millimetre to about 2·0 millimetres, and their histological appearance is shown in Figure III. There is no suggestion of condensation of tissue to form a wall; they are simply spaces caused by the œdema of the tumour substance. The same figure shows the histological structure of the bulk of the neoplasm—a fibrillary astrocytoma of quite low cellularity.

Sometimes the neoplastic growth may lead to a diffuse regular hypertrophy of some part of the brain (for examples see Latham, 1934). This is the so-called "gliomatosis".

In contrast to the inconspicuous astrocytomatous portion of the tumour was the conspicuous, firm tumorous mass of the thalamus. This was a typical anaplastic "*glioblastoma multiforme*" (Figure V). According to Scherer (1940*c*), in the majority of astrocytomata of the cerebrum, careful examination reveals areas of such anaplastic growth either macroscopically or microscopically. He did not regard the distinction between fibrillary and protoplasmic types as important, but said that the rather uncommon gemistocytic type might prove to be a type with distinctive biological features.

The cellularity of the tumour was determined by counting the number of cells in at least ten areas in both its portions, on sections 20μ thick of the astrocytomatous part, and 10μ thick of the more cellular part. Results are expressed for a section 20μ thick and a square of side 0·1 millimetre. The figures compare with those given by Scherer (1940*c*), if it is assumed that this was the area used by him, and not 0·1 square millimetre as he stated.

A point that does not seem to have received emphasis is that in descriptions of non-neoplastic astrocytes (for example, Jones, 1932; Biggart, 1949) it is usually stated that they divide by amitotic division and that mitosis is never seen, whereas authors writing about glial tumours, and tissue culture of these neoplastic cells, freely mention mitosis but scarcely refer to amitotic division.[1] In the anaplastic portion of the tumour here described both mitotic and amitotic division could be seen. In the multinucleated tumour giant cells, the origin of the nuclei by amitotic division could be seen from the many chromatin tails leading to a central point (Figure V).

In relation to the non-neoplastic included astrocytes in the anaplastic portion, a considerable number of which had

[1] There are exceptions such as Russell and Cairns (1930), who referred to amitotic division in their fibrillary cerebral astrocytoma.

become multinucleated, it should be noted that while a pale nucleus with prominent nucleolus is not possessed by normal astrocytes, such a nucleus is not diagnostic of a neuron under abnormal conditions, as abnormal astrocytes often have such a nucleus (Scherer, 1935*b*).

Invasion of the meninges by neoplastic cells of astrocytomatous type was seen in the region of the lateral sulcus and the orbital surface (Figure IV). This does not occur as commonly in astrocytomatous tumours as in "glioblastomatous" tumours that reach the surface, but even metastasis by the cerebro-spinal fluid may occur in a fibrillary astrocytoma (Russell and Cairns, 1930).

The invasion of the cortex in places and the disorganization of the internal architecture of the hemisphere by disruption of the basal nuclei are characteristic of astrocytomata. This contrasts with the peculiar behaviour not infrequently seen in "glioblastomata", which may spread through the white matter without disturbing the grey matter with which it is in contact (Scherer, 1940*a*). On the other hand, the nervous elements in the invaded tissue usually persist for longer in astrocytomata, although such persistence may sometimes be a feature in more anaplastic tumours.

In spite of the moderately large size of the anaplastic area which involved the thalamus, no necrosis was found. It has been pointed out by Scherer (1940*c*) that the lack of necrosis in "glioblastomatous" areas arising in conjunction with cerebral astrocytoma is in sharp contrast to the great degree of necrosis found in primary "glioblastomata".

It has long been recognized that the vessels of anaplastic glial tumours are peculiar, showing thickening of the adventitia and the intima (Figure VI). Hardman (1940), who studied the vascular architecture of gliomata, chiefly by thick sections in which the red corpuscles had been stained by Pickworth's method, regarded these vessels as being formed by dilatation of preexisting capillaries, with proliferation of the endothelium and of the adventitial cells, which are normally found in small numbers in association with the capillaries of the brain. On the other hand, Scherer (1935*c*), who made a very careful morphological study of the vessels, presented strong evidence that what is involved is a proliferation of capillary channels, leading to vascularization and thickening of the intimal or adventitial coat of existing vessels and also to the formation of new capillary tufts.

The clinical symptoms and death of this patient evidently were caused by the right-sided hydrocephalus resulting from blocking of the right intraventricular foramen by the anaplastic thalamic portion of the tumour. The widespread astrocytomatous growth must have been present for many years, because a great part of the white matter of the left hemisphere had disappeared, and lipoid-laden phagocytes were to be seen only in very small numbers.

The pathologist must give the surgeon all the help he can on the basis of biopsy material of glial tumours, but this material is quite inadequate for most research purposes. New knowledge and a better understanding of the gliomata can be gained only by a thorough and complete examination of necropsy material.

From the clinical point of view the case serves to emphasize the secondary effects that may give rise to false localizing signs, the chance blockage of the right interventricular foramen being far more productive of symptoms, at least in the terminal phases, than the large, long-standing glioma that occupied so much of the left-hand side of the brain.

Summary.

This paper is chiefly an exposition of the results obtained by Scherer on glial tumours by his "complete" method of investigation. For one of the most practical, concise and useful papers on gliomata yet published the reader is referred to "The Forms of Growth in Gliomas and Their Practical Significance" (Scherer, 1940*a*).

A case of fibrillary astrocytoma of the cerebrum with supervening anaplastic "glioblastomatous" growth is described. The features of cerebral astrocytomata are emphasized, together with the frequency with which "glioblastomatous" areas can be found in these tumours, and a plea is made for the recognition of the fact that it is only by thorough study of necropsy material that understanding of the gliomata can be advanced.

Acknowledgements.

The writer wishes to express his thanks to Dr. O. Latham for allowing him to examine and report the specimen, to Mr. T. Jones for preparing the sections, and to Mr. S. Woodward-Smith and Mr. K. Clifford for the photograph and photomicrographs.

References.

ADAMI, J. G., and NICHOLLS, A. G. (1911), "The Principles of Pathology", Second Edition, Lea & Febiger, Philadelphia, 2 : 593.

BAILEY, P. (1933), "Intracranial Tumors", Thomas, Springfield.

BAILEY, P. (1948), "Intracranial Tumors", Second Edition, Thomas, Springfield.

BAILEY, P., and CUSHING, H. (1926), "A Classification of the Tumors of the Glioma Group on a Histogenic Basis with a Correlated Study of Prognosis", Lippincott, Philadelphia.

BIGGART, J. H. (1949), "Pathology of the Nervous System. A Student's Introduction", Second Edition, Livingstone, Edinburgh, 19.

CAIRNS, H., and RUSSELL, D. S. (1931), "Intracranial and Spinal Metastases in Gliomas of the Brain", *Brain*, 54 : 377.

CARMICHAEL, E. A. (1928), "Cerebral Gliomata", *J. Path. & Bact.*, 31 : 493.

COURVILLE, C. B. (1950), "Pathology of the Central Nervous System", Third Edition, Pacific Press, Mountain View, 403.

COX, L. B. (1933), "The Cytology of the Glioma Group; with Special Reference to the Inclusion of Cells Derived from the Invaded Tissue", *Am. J. Path.*, 9 : 839.

COX, L. B., and CRANAGE, M. L. (1937), "Studies on the Tissue Culture of Intracranial Tumours", *J. Path. & Bact.*, 45 : 477.

CUSHING, H. (1931), "Experiences with the Cerebellar Astrocytomas. A Critical Review of Seventy-six Cases", *Surg., Gynec. & Obst.*, 52 : 129.

EWING, J. (1940), "Neoplastic Diseases", Fourth Edition, Saunders, Philadelphia, 440.

GRINKER, R. R., and BUCY, P. C. (1949), "Neurology", Fourth Edition, Thomas, Springfield, 437.

HARDMAN, J. (1940), "The Angioarchitecture of the Gliomata", *Brain*, 63 : 91.

JONES, O. W. (1932), "Cytogenesis of Oligodendroglia and Astrocytes", *Arch. Neurol. & Psychiat.*, 28 : 1030.

KERNOHAN, J. W., MABON, R. F., SVIEN, H. J., and ADSON, A. W. (1949), "A Simplified Classification of the Gliomas", *Proc. Staff Meet., Mayo Clinic*, 24 : 71.

LATHAM, O. (1934), "Some Activities of a Mental Hospital Laboratory During Thirty Years" (The Beattie-Smith Lectures), M. J. AUSTRALIA, 1 : 746.

MUNRO, D., EDWARDS, J. E., and RUSSELL, W. O. (1941), "Mixed Intracranial Gliomas", *Surg., Gynec. & Obst.*, 72 : 787.

RIBBERT, H. (1918), *"Über das Spongioblastom und das Gliom"*, *Arch. path. Anat.*, 235 : 195.

RINGERTZ, N. (1950), "'Grading' of Gliomas", *Acta path. et microbiol. scandinavica*, 27 : 51.

RUSSELL, D. S., and BLAND, J. O. W. (1933), "A Study of Gliomas by the Method of Tissue Culture", *J. Path. & Bact.*, 36 : 273.

RUSSELL, D. S., and BLAND, J. O. W. (1934), "Further Notes on the Tissue Culture of Gliomas with Special Reference to Bailey's Spongioblastoma", *J. Path. & Bact.*, 39 : 375.

RUSSELL, D. S., and CAIRNS, H. (1930), "Spinal Metastases in a Case of Cerebral Glioma of the Type Known as Astrocytoma Fibrillare", *J. Path. & Bact.*, 33 : 383.

SCHERER, H. J. (1935*a*), *"Gliomstudien. I. Problemstellung. Methodik"*, *Arch. path. Anat.*, 294 : 790.

SCHERER, H. J. (1935*b*), *"Gliomstudien. II. Über die Grenzen der Zelldiagnostik in Gehirngeschwülsten, dargestellt am Beispiel des 'Glioblastoma multiforme ganglioides'"*, *Arch. path. Anat.*, 294 : 795.

SCHERER, H. J. (1935*c*), *"Gliomstudien. III. Angioplastische Gliome"*, *Arch. path. Anat.*, 294 : 823.

SCHERER, H. J. (1938), "Structural Development in Gliomas", *Am. J. Cancer*, 34 : 333.

SCHERER, H. J. (1940*a*), "The Forms of Growth in Gliomas and Their Practical Significance", *Brain*, 63 : 1.

SCHERER, H. J. (1940*b*), "The Pathology of Cerebral Gliomas", *J. Neurol. & Psychiat., New Series*, 3 : 147.

SCHERER, H. J. (1940*c*), "Cerebral Astrocytomas and Their Derivatives", *Am. J. Cancer*, 40 : 159.

SVIEN, H. J., MABON, R. F., KERNOHAN, J. W., and ADSON, A. W. (1949), "Astrocytomas", *Proc. Staff Meet., Mayo Clin.*, 24 : 54.

WILLIS, R. A. (1948), "Pathology of Tumours", Butterworth, London.

WILSON, S. A. K. (1940), "Neurology", Arnold, London, 2 : 1178.

Legends to Illustrations.

FIGURE III.—Microcystic degeneration. The typical picture of a fibrillary astrocytoma can be seen, with numerous spaces in the tissue without condensation of glial fibres to form a wall. (Masson's stain, × 185.)

FIGURE IV.—Meningeal invasion. Obliteration of the posterior ramus of the lateral sulcus has occurred at this point by invasion from fibrillary astrocytomatous tissue (below). (Hæmatoxylin and eosin stain, × 150.)

FIGURE V.—Section of left thalamus showing the histological picture of *"glioblastoma multiforme"*. The many nuclei of the neoplastic giant cell are connected by tails to a central point, indicating an origin by amitotic division. (Hæmatoxylin and eosin stain, × 375.)

FIGURE VI.—Blood vessels in the anaplastic part of the tumour. The typical, conspicuous, irregularly thickened appearance of the vascular channels can be seen. Red blood corpuscles are stained black. (Phosphotungstic acid hæmatoxylin stain, × 150.)

FIGURE VII.—Early perivascular secondary structures (for explanation see text). Lines of tumour cells can be seen along the vessels. From the neighbourhood of an area of fibrillary astrocytomatous tissue in the subcortical white matter of the frontal lobe. Such secondary structures are more typical of anaplastic tumour cells (*"glioblastoma multiforme"*). (Hæmatoxylin and eosin stain, × 150.)

THE USE OF PARALDEHYDE IN ALCOHOLIC DELIRIUM TREMENS.

By DOUW G. STEYN, B.Sc., Dr.Med.Vet., D.V.Sc.,
Department of Pharmacology, University of Pretoria, Pretoria, Union of South Africa.

THE treatment of alcoholic *delirium tremens* with paraldehyde in a case in which I was recently consulted once more brought home to me very forcibly the urgency of reconsidering the use of this sedative in the treatment of the above disease.

It is not my intention to give a complete review of our knowledge of the pharmacological and toxicological actions of paraldehyde, but only to mention and discuss the most salient points as far as the use of this drug in the treatment of alcoholic *delirium tremens* is concerned.

Actions, Uses and Therapeutic Doses of Paraldehyde.

It is unnecessary to give details about the doses and methods of administration of paraldehyde, as these are to be found in all books on pharmacology, pharmacopœias *et cetera* (Bastedo, 1947; British Pharmaceutical Codex, 1944; Clark, 1952; Cushny, 1947; Eichholtz, 1947; Phillips, 1952; Sollman, 1948; United States Dispensatory, 1947).

Sollman (1948) states that "the margin of safety on intravenous injection is narrow in animals". According to Burstein (1943), "paraldehyde administration intravenously is not as safe as is generally believed", while Burstein and Rovenstine (1941) state that "the intravenous administration of paraldehyde as recommended for clinical anæsthesia is not without danger".

Wechsler (1940) administered, with success, one cubic centimetre of paraldehyde intravenously in violent restlessness and convulsions of prolonged duration which did not respond to other treatment. In serious cases this dose could be repeated.

Paraldehyde is used (i) as a hypnotic, (ii) to produce analgesia and amnesia in labour, and (iii) as a general anæsthetic agent for short operations, or as a pre-anæsthetic agent for longer ones. Its chief use is to tranquillize delirious patients.

Carmichael *et alii* (1944) established that guinea-pigs injected intraperitoneally with paraldehyde developed a tolerance to it as indicated by both sleeping time and length of hypnosis. This phenomenon is of significance, as after repeated administration of paraldehyde, patients will require progressively larger quantities in order to achieve the desired sedative and hypnotic effects, and consequently dangerous doses may be administered.

Phillips (1952) suggests a method for preparing a mixture which does away with the unpleasant nature of this drug for the patient and circumvents the difficulties encountered in its dispensing.

Toxic and Fatal Doses of Paraldehyde.

Bastedo (1947) "observed a death from four doses of 15 c.c. (½ ounce) by rectum, given through the night to an alcoholic". Clark (1952), referring to paraldehyde, states that "the B.P. dose is 2 to 8 ml., but a dose of 8 ml. is likely to produce intoxication and to aggravate the excitement in a delirious patient". According to him "a few deaths have occurred with doses of 30 ml., but recoveries have occurred after doses of 100 ml.".

Three fatal cases of paraldehyde poisoning are described in an editorial in *The Lancet* (1947). Two patients in a mental hospital died as a result of an accident through overdosage. Each of them received two fluid ounces (60 cubic centimetres) of pure paraldehyde. Both died in spite of gastric lavage, artificial respiration and oxygen inhalations.

Eichholtz (1947) refers to the appearance of *delirium tremens* after the therapeutic use of paraldehyde. In one of Glaister's (1945) cases death resulted from overdosage. The patient received rectally five ounces of paraldehyde instead of five drachms. Leschke (1934) quotes two deaths which occurred after the ingestion of 25 and 52 grammes of paraldehyde respectively.

Hemphill and Heller (1945) describe severe and alarming toxic reactions following the administration of 120 minims (approximately eight cubic centimetres) of paraldehyde to seven of nine mental patients. The toxicity of the suspected paraldehyde was tested on mice, but it was found not to possess increased toxicity. The clinical picture was similar to severe intoxication with ethyl alcohol with a more prolonged "hangover".

Lehmann and Flury (1943) state that the symptoms of chronic paraldehyde poisoning are similar to those seen in chronic alcohol poisoning.

Sapeika (1949) states that paraldehyde "sometimes produces habit and *delirium tremens*".

Schneider (1937) quotes a case in which a female patient in an asylum died after having received 40 to 50 grammes of paraldehyde instead of four grammes. Schoor (1941) describes fatal poisoning in a healthy *primipara* (twenty-one years old) who had received 12 cubic centimetres of paraldehyde in six cubic centimetres of benzyl alcohol and 30 cubic centimetres of physiological saline solution rectally. One and a half hours before death she had generalized convulsions. Kotze, quoted by Schoor (1941), reports the death after 31 cubic centimetres of paraldehyde of a patient with pregnancy toxæmia.

According to Sollmann (1948) addiction to paraldehyde "presents the phenomena of chronic alcoholism, including *delirium tremens*". In reply to a question in the *British Medical Journal* (1947) it is stated that "in rare cases of true addiction to paraldehyde the symptoms may be indistinguishable from those of chronic alcoholism. Even *delirium tremens* has been reported".

Furthermore, in an editorial in the *British Medical Journal* (1945) referring to paraldehyde, it is stated that "unfortunately, however, alcoholics are more than usually tolerant of this drug, and it may produce not the desired sleep but only increasing restlessness".

Factors and Conditions which Increase the Toxicity of Paraldehyde.

Paraldehyde.

Paraldehyde decomposes under different conditions of storage, and Toal (1937) states that it "will not remain stable under the practical conditions of everyday use". He suggests that it is essential to add preservatives to paraldehyde as it does not keep under commercial and dispensary conditions. As preservatives for paraldehyde, α-naphthol, β-naphthol, diphenylamine and hydroquinone have been recommended. In white bottles decomposition

of paraldehyde is quicker than in amber-coloured bottles, and air-spaces in the bottles accelerate decomposition of this drug.

On decomposition of paraldehyde peroxidized compounds are formed, and there are also an increase in acidity and a higher boiling-point beyond the limits of the British Pharmacopœia. However, according to Hemphill and Heller (1945) the increase in the toxicity of paraldehyde on decomposition may be due, not to acid or peroxidized substances, but to other decomposition products.

Brester (1948*a*) discusses the control of the purity and toxicity of paraldehyde, and states that the testing of paraldehyde by the permanganate test of the Dutch pharmacopœia is not reliable, and that this test should be replaced by the test for peroxide (*Pharmacopœia Helvetia*, Fifth Edition) and for acetaldehyde (United States Pharmacopœia, Thirteenth Edition). According to his tests, Brester (1948*b*) found that paraldehyde in partly-filled brown bottles had deteriorated, and suggested that such bottles should not be stored for longer than two weeks. He also proposed that the instruction in the *Pharmacopœia Helvetia* to store paraldehyde in fully-filled bottles should be adopted in the revision of pharmacopœias.

Marston and Allchin (1942) state that for intramuscular injection paraldehyde may be sterilized by being heated at 130° C. for thirty minutes and kept in amber glass ampoules. He continues: "Paraldehyde for sterilization should not contain free acid equivalent to more than 0·1 mil of N/10 sodium hydroxide and should not be allowed to come into contact with rubber during storage."

The Patient: The Condition of the Liver.

According to the investigations of Levine *et alii* (1939, 1940) in the normal animal, 70% to 88% of the paraldehyde administered is destroyed in the body, according to the dose, and the lungs excrete the major part of the drug not combusted in the body. In their experiments (Levine *et alii*, 1940) 11% to 28% of the paraldehyde administered (1·0 to 2·0 millilitres per kilogram) was excreted by the lungs, and only 0·1% to 2·5% by the kidneys. The results of their experiments upon dogs confirmed (i) the experience that the liver plays an important role in the destruction of paraldehyde, and (ii) that a damaged liver (chloroform anæsthesia) renders the animals more susceptible to paraldehyde. They rightly concluded that hepatic insufficiency is a contraindication to the clinical use of paraldehyde. Hitchcock and Nelson (1943) found that mice which had received carbon tetrachloride in addition to paraldehyde, excreted the latter through the lungs for much longer periods than mice which had received paraldehyde only. As carbon tetrachloride is an active liver poison which inhibits liver function, paraldehyde remained much longer in the body. According to Sollmann (1948), "hepatic insufficiency causes a longer and higher blood-concentration curve of paraldehyde, presumably by slowing the destruction". Bodansky *et alii* (1941) quote figures for blood-aldehyde concentrations in patients who had received this drug. They state that dogs were promptly revived from paraldehyde poisoning by "Metrazol". In spite of the fact that paraldehyde has been, and is still, widely used as a sedative in *delirium tremens*, I feel that it should not be the drug of first choice in cases of alcoholic *delirium tremens*, as there is evidence that it may aggravate the delirium instead of inducing sedation.

Treatment of Alcoholic Delirium Tremens.

Paraldehyde, choral hydrate, bromides, alcohol and the barbiturates are cortical depressants. Paraldehyde has been, and is still being, extensively used in the treatment of alcoholic *delirium tremens*. However, in the light of our knowledge of the pharmacological and toxicological properties of paraldehyde, I am in full agreement with the following statement made by Minogue (1952): "Paraldehyde acts as a cerebral excitant in alcoholics, and I have abandoned its use in these cases." This is a most significant statement coming from a man of the calibre of Minogue who, owing to his experience in the treatment of alcoholics, was requested by the Editor of THE MEDICAL JOURNAL OF AUSTRALIA to write an article on *delirium tremens*. In his article Minogue supplies full details of the treatment of alcoholic *delirium tremens*. The information is most important and the article should be consulted for full details of the various drugs used, their dosages and the methods, intervals and periods of administration. The drugs used by Minogue are pentobarbital sodium and "Carbrital" (carbromal with pentobarbital sodium) in mild cases, and in more serious cases hypodermic injections of hyoscine hydrobromide (1/100 to 1/150 grain), morphine sulphate (1/4 to 1/6 grain), and atropine sulphate (1/120 grain); this injection may be repeated in three to four hours. A significant feature in Minogue's treatment is that when the patient wakes up after the above-mentioned injection and is still hallucinated, he is given an ounce of brandy every three or four hours until the hallucinations disappear. The use of muscle relaxants (mephenesin, "Myanesin" *et cetera*) is rightly suggested to control the tremors. I was particularly pleased to see that Minogue included in his regimen of treatment insulin and glucose (10 units of insulin given three times daily, followed half an hour later by 50 grammes of glucose) and thiamin, and that he recommends copious amounts of fruit juices and water and no restriction on diet. It is reported by several authors (Editorial, 1945) that insulin and glucose are of great value in the treatment of *delirium tremens*. The best results are achieved when glucose is administered two and a half hours after the insulin (40 to 80 units). A great advantage of insulin administration is the marked improvement in appetite, which is of such great importance in these starved patients. It is stated that the average stay in hospital is halved. As alcoholics are sick and underfed people suffering from complex deficiencies (protein, mineral and vitamin) chiefly as a result of lack of appetite, I am convinced that they would derive great benefit from treatment which included in their daily adequate diet one ounce of food yeast to increase their intake of the *B* complex vitamins and proteins and also to improve their appetite. High-value protein is of extreme importance. As thiamin and glutamic acid are valuable brain "foods", and as normal liver function is seriously disturbed in chronic alcoholics, it is advisable that *delirium tremens* patients receive these two dietary factors in addition to an adequate diet. Perhaps it would be of value also to include choline, methionine and glutathione as foods for the cirrhotic liver for a brief period, especially in cases of fatty liver. I am fully aware of the differences of opinion as to the value of glutamic acid as a brain "food", but I believe that, owing to the disturbed protein metabolism as a result of the liver affection in chronic alcoholics, there is a possibility that such patients are likely to derive benefit from these two foods if they are given during the acute stages of the disease. Not only is thiamin essential to normal metabolism in nerve tissue, but it is well known that the requirements of thiamin for the alcoholic are much higher than for a normal individual.

I should like to add that I am fully conscious of the dangers of administering individual food factors to patients over long periods; but I believe that there are times and occasions when such treatment, if applied in the correct manner, will benefit the patient. This method of using food factors naturally carries us from the domain of nutrition into pharmacology, and all therapeutic substances have to be used with due care.

Regarding the use of sedatives in the treatment of *delirium tremens* Minogue (1952) makes the following statement:

> On the whole, however, sedatives and hynotics are best avoided. Too many of these patients give up alcohol only to become addicted to the barbiturates, bromides, or chloral hydrate, which they take in increasing doses, and their last state is worse than their first.

It is gratifying to see that Minogue (1952) states that hospital treatment for *delirium tremens* is best. The very serious problem of the chronic alcoholic would certainly be less of a nightmare to the medical practitioner if he had the necessary hospital facilities for treating his patients. Furthermore, proper treatment of such patients in hospital would certainly yield much better results than treatment

under existing conditions. Not only would many lives which are at present lost be saved, but the chances of curing the alcoholic from his craving for alcohol would be infinitely better.

Discussion.

From the foregoing facts and discussions it appears obvious that, as far as drug treatment of alcoholic *delirium tremens* is concerned, paraldehyde should be completely excluded from the regimen of treatment of such patients, for the following reasons: (i) Alcoholics are more tolerant than others of the sedative effects of this drug and it may, and does, at times produce increased restlessness instead of sedation. (ii) It is inclined to aggravate alcoholic *delirium tremens* instead of tranquillizing the patient. (iii) On account of the advanced liver affection in alcoholics, they possess an increased susceptibility to the toxic action of paraldehyde. As a matter of fact, owing to the synergistic pharmacological and toxicological effects of paraldehyde and alcohol, and especially the inclination of the former to aggravate alcoholic *delirium tremens*, the use of this drug is contraindicated, rather than indicated, in the treatment of this malady. Furthermore, paraldehyde causes toxic hepatitis (United States Dispensatory, 1947), and to administer an active liver poison to a patient already suffering from a severely damaged liver, as is the case in the alcoholic, certainly seems most dangerous and undesirable.

Owing to increased tolerance in the alcoholic to paraldehyde, one is in great danger of increasing and repeating the dose in order to achieve sedation, whilst not realizing that the increase in excitement and delirium after paraldehyde administration may be, and probably is, due to the synergistic effect of paraldehyde.

The great importance of an adequate diet, containing especially high-value protein and food yeast, in the treatment of alcoholics is stressed. It is suggested that during acute attacks thiamin, glutamic acid, methionine, glutathione and choline be administered for short periods to alcoholics, as, owing to the defective liver function, they will probably benefit by such treatment. Insulin injections and glucose administration halve the period of hospital retention of *delirium tremens* patients. As sedatives in alcoholic *delirium tremens*, it is suggested that barbiturates (for example, pentobarbital sodium), morphine and hyoscine be used, as suggested by Minogue (1952).

References.

ANY QUESTIONS? (1947), "Paraldehyde Addiction", *Brit. M. J.*, 1 : 957.

BASTEDO, W. A. (1947), "Pharmacology, Therapeutics and Prescription Writing", Saunders, London.

BODANSKY, M., JINKINS, J. L., LEVINE, H., and GILBERT, A. J. (1941), "Clinical and Experimental Studies on Paraldehyde", *Anesthesiology*, 2 : 20.

BRESTER, A. (1948*a*), *"Enige mededelingen over paraldehyde", Pharmaceut. Weekbl.*, 83 : 9.

BRESTER, A. (1948*b*), *"Verdere mededelingen over paraldehyde", Pharmaceut. Weekbl.*, 83 : 193.

"BRITISH PHARMACEUTICAL CODEX", 1944.

BURSTEIN, C. L., and ROVENSTINE, E. A. (1941), "Toxicity of Intravenous Paraldehyde", *Proc. Soc. Exper. Biol. & Med.*, 48 : 669.

BURSTEIN, C. L. (1943), "The Hazard of Paraldehyde Administration: Clinical and Laboratory Studies", *J.A.M.A.*, 121 : 187.

CARMICHAEL, E. B., KAY, F. A., and PHILLIPS, G. W. (1944), "Studies on Guinea Pigs after Repeated Administration of Paraldehyde", *Proc. Soc. Exper. Biol. & Med.*, 55 : 22.

CLARK, A. J. (1952), "Applied Pharmacology", Eighth Edition, Churchill, London.

CUSHNY, A. R. (1947), "Pharmacology and Therapeutics", Thirteenth Edition, Churchill, London.

EDITORIAL (1945), "Insulin for Delirium Tremens", *Brit. M. J.*, July 21, p. 91-92.

EICHHOLTZ, F. (1947), *"Lehrbuch der Pharmakologie"*, Fifth Edition, Springer-Verlag, Berlin.

GLAISTER, J. (1945), "Medical Jurisprudence and Toxicology", Livingstone, Edinburgh.

HITCHCOCK, P., and NELSON, E. E. (1943), "The Metabolism of Paraldehyde", *J. Pharmacol. & Exper. Therap.*, 79 : 294.

LEHMANN, K. B., and FLURY, F. (1943), "Toxicology and Hygiene of Industrial Solvents", Williams and Wilkins, Baltimore.

LESCHE, F. (1934), "Clinical Toxicology", Churchill, London.

LEVINE, H., GILBERT, A. J., and BODANSKY, M. (1939), "The Effect of Liver Damage on the Blood Level and Action of Paraldehyde", *J. Pharmacol. & Exper. Therap.*, 67 : 299.

LEVINE, H., GILBERT, A. J., and BODANSKY, M. (1940), "The Pulmonary and Urinary Excretion of Paraldehyde in Normal Dogs and in Dogs with Liver Damage", *J. Pharmacol. & Exper. Therap.*, 69 : 316.

MARSTON, A. E., and ALLCHIN, J. P. (1942), "Injections of Paraldehyde", *J. Pharmacol.*, 149 : 152.

"MEDICINE AND THE LAW" (1947), "Overdose of Paraldehyde", *Lancet*, 1 : 188.

MINOGUE, S. J. (1952), "Delirium Tremens", M. J. AUSTRALIA, 2 : 254.

PHILLIPS, M. F. (1952), "Paraldehyde Administration: A Suggestion", *Pharmaceut. J.*, 169 : 206.

SAPEIKA, N. (1949), "Actions and Uses of Drugs", Balkema, Cape Town.

SCHNEIDER, P. (1937), *"Veränderungen der Magenschleimhaut bei tödlicher Paraldehyd-Vergiftung", Samml. Vergiftungsfällen*, 8 : 103.

SCHOOR, M. (1941), "Paraldehyde Poisoning", *J.A.M.A.*, 117 : 1534.

SOLLMAN, T. (1948), "A Manual of Pharmacology", Saunders, London.

TOAL, J. S. (1937), "The Decomposition of Paraldehyde B.P. on Storage", *Quart. J. Pharmacy and Pharmacol.*, 10 : 439.

"UNITED STATES DISPENSATORY" (1947), 822.

WECHSLER, I. S. (1940), "Intravenous Injection of Paraldehyde for the Control of Convulsions", *J.A.M.A.*, 114 : 2198.

A SUMMARY OF ALL CASES OF ANTE-PARTUM HÆMORRHAGE IN THE PUBLIC SECTION OF THE BRISBANE WOMEN'S HOSPITAL DURING THE PERIOD FROM JULY 1, 1951, TO JUNE 30, 1952.

By J. F. DUNKLEY, M.B., B.S. (Melbourne),

AND

R. THATCHER, M.R.C.S., L.R.C.P., M.R.C.O.G.,

Brisbane.

As part of a research scheme in this hospital it was decided that all public patients who developed ante-partum hæmorrhage should be cared for by one clinic during one year. For this reason we have had an opportunity to examine and follow up 48 patients with ante-partum hæmorrhage in one year. A careful survey of the reported cases was made to exclude small and insignificant hæmorrhages occurring by way of a "show" on the day of delivery.

The causative factors are shown in Table I.

TABLE I.

Cause of Hæmorrhage.	Number of Cases.	Living Children.	Stillbirths.	Neonatal Deaths.
Placenta prævia ..	19	20[1]	0	2
Toxæmia ..	17	12	5	2
Traumatic and other causes[2] ..	12	9	3	0
Total	48	41	8	4

[1] One pair of twins.

[2] Traumatic and other causes included the following: possible lateral *placenta prævia* (6), possible toxæmic ante-partum hæmorrhage (3), cervical erosion (1), decidual or placental disease (2).

There were no maternal deaths. The average stay in hospital before delivery was twelve days and the longest stay nine weeks. The total number of admissions to the public section of the hospital in this time was 3165.

Placenta Prævia.

The criteria required for the diagnosis of *placenta prævia* were palpation or direct vision of the placenta at operation, or evidence of separation of the border of the placenta in close relation to the hole in the membranes after delivery.

Four central, four marginal and eleven lateral *placentæ prævieæ* were seen. All patients with central or marginal *placenta prævia* were treated by Cæsarean section, with the exception of one who had a marginal *placenta prævia* and

was delivered safely after artificial rupture of the membranes during labour. Patients with lateral *placenta prævia* were treated by artificial rupture of the membranes during labour on three occasions, and by the allowing of spontaneous labour and delivery on eight occasions. Cæsarean section was carried out on one elderly *primipara* in whom gross distress of the fœtus occurred. This was later shown to be due to five turns of the cord round the neck.

Toxæmic Ante-partum Hæmorrhage.

The criteria for the diagnosis of toxæmic ante-partum hæmorrhage were the absence of obvious evidence of *placenta prævia* and a blood pressure of at least 150 millimetres of mercury, systolic, and 90 millimetres, diastolic, with or without albuminuria.

Treatment was by artificial rupture of the membranes in six cases, and medical induction was carried out in five cases, in which it was considered that no damage to the uterine muscle had occurred, as evidenced by lack of abdominal tenderness. The remaining patients delivered themselves spontaneously within forty-eight hours of their admission to hospital.

Traumatic Ante-partum Hæmorrhage and That due to Other Causes.

Of the third group, nine patients delivered themselves spontaneously, and two were delivered after artificial rupture of the membranes.

Principles of Treatment Adopted.

Placenta Prævia.

On the patient's admission to hospital the resident medical officer was instructed as a routine procedure to institute the following measures: (i) The application of rest and warmth, with the foot of the bed raised, and the administration of a quarter of a grain of morphine for restlessness and continued hæmorrhage. (ii) Recording of the blood pressure and pulse rate every half-hour, or more frequently if necessary, till the systolic blood pressure reached 100 millimetres of mercury. (iii) Blood grouping, hæmoglobin estimation and cross-matching of blood if necessary. (iv) Examination of the abdomen—no pelvic examinations. (v) Transfusion as necessary. (vi) Immediate notification of the obstetrician concerned.

Active interference in cases of suspected *placenta prævia* was avoided unless dangerous hæmorrhage continued, or unless a central *placenta prævia* was suspected in a patient who had a pregnancy corresponding to a maturity of thirty-six weeks both in dates and in size.

A speculum examination was made if small hæmorrhages recurred, to exclude vaginal or cervical causes of bleeding.

Vaginal examinations were made by the obstetrician only, and were directed to finding whether the placenta presented in front of or with the leading part of the fœtus. No attempt was made to search the lower segment. This examination was not made in the operating theatre as a rule.

When the presenting part was engaged in the pelvis in any case of *placenta prævia* instructions were left for the resident medical officer to carry out pelvic examinations as required for delivery, to rupture membranes and to apply a firm abdominal binder if bleeding was troublesome while labour proceeded. No medical or surgical inductions were allowed, and "Pitocin" was not given at any time.

The third stage was carefully watched, "Pitocin" and ergometrine being given after its completion.

The placenta and membranes were inspected and observations were recorded.

Toxæmic Ante-partum Hæmorrhage.

In toxæmic ante-partum hæmorrhage the same instructions were given on the patient's admission to hospital.

All patients with toxæmic ante-partum hæmorrhage who did not come into labour spontaneously within forty-eight hours of their admission to hospital had the membranes ruptured if uterine tone was good. No "Pitocin" was given to any patient with suspected damage to the uterine muscle. Medical induction was used only for the few cases in which rupture of the membranes was not sufficient and the toxæmia was severe.

No patient in the series presented the clinical features of a non-contracting uterus, which would have demanded Cæsarean hysterectomy.

Observations.

Central *placenta prævia* caused malpresentation or failure of engagement of the fœtal head in every case.

The distinction between central, marginal and lateral *placenta prævia* is of little practical value and could well be altered to presenting placenta and lateral placenta. This corresponds with the fact that hæmorrhage is easily controlled by rupture of the membranes during labour in the latter, while in the former Cæsarean section is a *sine qua non* if the baby is alive and viable and the patient in a suitable hospital.

Lower segment Cæsarean section presented no difficulty in this series.

Cystography was found to be of little practical value except when findings were negative.

Two patients with central *placenta prævia* being treated expectantly, whose final diagnosis was not made, had severe hæmorrhages and required resuscitation and transfusion before or during operation.

No patient with toxæmic ante-partum hæmorrhage was treated by Cæsarean section.

Blood transfusion was given as a routine measure in all cases at Cæsarean section.

Vaginal examinations should never be performed except by the obstetrician himself, and in a hospital where Cæsarean section can be undertaken safely. The finger is passed through the os only after palpation of the vaginal fornices. No attempt is made to search the lower segment of the uterus. In suspected *placenta prævia* such an examination is made at the thirty-sixth week to verify or exclude a presenting placenta.

Acknowledgement.

We wish to thank the Medical Superintendent of the Brisbane Women's Hospital for permission to publish this paper.

AIR EVACUATION OF CASUALTIES IN THE KOREAN WAR.

By N. M. KATER, M.C.,
Wing Commander, Royal Australian Air Force, Sydney.

SINCE the Korean war commenced, air evacuation of casualties has developed to such an extent that today it is the primary means of patient movement, and nearly every patient who leaves Korea travels by air.

This is a very different state of affairs from that which existed in July and August, 1950, when the Communists threatened to overrun all Korea; at that time the wounded were taken back to Japan by any method available. Many were flown out, but large numbers went by L.S.T., Japanese merchant vessels, Chinese junks, and anything else that floated.

So far has air evacuation proceeded in the United States Armed Forces that it is stated that today not a single hospital train is running in the United States, and no hospital ship carries patients across the seas.

The United States hospital ships now stationed in Korea serve as floating base hospitals, and all casualties are carried by air from Japan to the United States. The aircraft used are "Skymasters" and "Stratocruisers"; the

latter are able to carry 60 patients and to deliver a wounded man in the United States in twenty-six hours.

During 1951 many of the United States wounded were flown from Japan to the United States.

During the last war approximately 4% of wounded who reached their regimental aid posts or battalion aid stations died; in the Korean war this figure has been reduced to 2%, the chief reasons being air evacuation, increased and earlier use of blood and more antibiotics.

Air evacuation for many wounded begins in a helicopter, which picks them up from a forward position, and ends as far as the United States Army is concerned when the casualty reaches the United States.

The Royal Australian Air Force is bearing its share of air evacuation, and is evacuating all casualties from the First Commonwealth Division from Korea to Japan.

The Royal Australian Air Force uses "Dakota" aircraft, which carry 24 litter patients or 27 ambulant patients; a nursing sister and a medical orderly are carried on all trips.

The aircraft are based at Iwakuni in Japan and pick up the patients in Korea. Food is carried for the patients on the journey, which takes between three and four hours.

All types of casualties are carried, and all travel well by air at the heights flown, which rarely exceed 8000 feet. Oxygen is occasionally required for patients with chest wounds, and for some with medical conditions.

Dinghys sufficient to carry the crew and patients in case of a forced landing in the sea are carried.

In the winter hot air is blown into the cabin of the aircraft before it takes off from Korea.

After arrival at Iwakuni the patients are fed and proceed by train to a British General Hospital at Kure; this takes about two and a half hours. Air evacuation for the Australian and New Zealand patients goes further; they are evacuated to Australia by Qantas "Skymaster", and are looked after by a Royal Australian Air Force nursing sister and medical orderly *en route*.

The air evacuation sisters and orderlies are trained for the job and do a special course in air evacuation before being posted to Japan.

Air evacuation aircraft fly in all weathers, and only on rare occasions are they unable to get through.

Acknowledgement.

I desire to thank the Director-General of Medical Services, Royal Australian Air Force, Air Vice-Marshal E. A. Daley, C.B.E., Q.H.P., for permission to publish this paper.

CONTINUOUS IMMOBILIZATION OF JOINTS IN RHEUMATOID ARTHRITIS.[1]

By MICHAEL KELLY,
Melbourne.

Rheumatoid arthritis is the least amenable to surgical intervention, but will, doubtless, in future be a more docile disease in the hands of the physician, who should from the first recognize that the deformities of the limbs may be prevented by simple mechanical devices, and this is most important, especially in the knees.

—SIR ROBERT JONES (1909).

THE better to placate this distinguished assembly of orthopædic surgeons, I open with words written by the greatest orthopædic surgeon of them all.

I am going to state to you a few opinions which I formed, painfully and laboriously, in general practice in the country. Joints are of perennial interest to the general practitioner, and I had had my interest stimulated during a short association with Dr. Lionel Betts, of Adelaide, an orthopædic surgeon who had himself practised in the country, and who always retained a broad outlook on medicine. For a time I wanted to be an orthopædic surgeon; then I could see that there was a field for an orthopædic physician. Orthopædic principles are not confined to orthopædic surgery; if they are right they belong to the whole of medicine, and they should especially be the province of the physician who treats articular disorders.

When "Cellona" plaster of Paris came on the market I developed the routine of putting all sprained wrists, fingers and toes, and most of the sprained knees and ankles, in plaster, and it was remarkable how quickly they recovered. From these it was but a short step to non-traumatic synovitis, and later I found myself immobilizing many acute rheumatic and rheumatoid joints. The results were fairly good; but on looking back I can see that, through fear of anylosis, I did not immobilize them for long enough. During the last few years I have had opportunities of studying the method more closely, and I have found no reason for modifying my earlier opinion; rather it has been strengthened and developed into an important principle which should never be forgotten.

An Important Principle.

This is the important principle: "As far as it is technically possible and consistent with use of the limb, every painful and swollen joint should be immobilized continuously for at least three weeks." That principle has been accepted since the days of John Hunter, but in the treatment of rheumatoid joints it has not been carried out through fear of ankylosis. However, I have been able to find no factual evidence that ankylosis is hastened by immobilization. Rather it is argued theoretically that it would happen, because ankylosis often occurs even when the joints are not immobilized.

But the joints do not become ankylosed. On the contrary, ankylosis is prevented. The periarticular swelling and synovial thickening subside forthwith, and the synovial fluid disappears in a remarkably short time. The pain and tenderness—the patient's chief and often only complaints—also disappear instantly. Within a few days the appearance of the joint returns to normal; but the plaster should be kept on for three to five weeks in order to minimize the danger of recurrence. Then only the gentlest active movements, within painless range, are required to bring full movements back; full range usually returns in two or three weeks. The joint should be splinted intermittently during this time.

Usually the range of movement three weeks after the plaster splint has been removed is greater than it was before the plaster splint was put on. This may seem a strange paradox, but it is consistent with the known pathology of rheumatoid arthritis. A painful and swollen joint is stiff because (i) it is painful to move, (ii) the articular and periarticular tissues are less mobile, (iii) the muscles are spastic. When it is no longer painful and swollen it is less likely to be stiff. The cause of rheumatoid arthritis is not known; but movement contributes to the painful swelling of the joints—and movement perpetuates the vicious circle.

Ankylosis an End-Result of Recurring Articular Damage.

Ankylosis is a common end-result of rheumatoid arthritis; but there is no special ankylosing quality about the rheumatoid inflammation as such. It is a non-specific cellular reaction which cannot be distinguished from the effects of injury. As long as the inflamed and friable tissues are moved they will become more inflamed and more friable. Ligaments become œdematous, cartilage is destroyed, bone is decalcified and softened. Tendons become adherent, muscles waste away and their balance is altered, and they are unable to resist such external forces as gravity. Ankylosis is usually preceded by deformity, and these are the factors which go to produce deformity.

If, on the other hand, the injured articular tissues are put at rest, the inflammatory process goes into reverse.

[1] Read at a meeting of the Section of Orthopædics and Physical Medicine, Australasian Medical Congress (British Medical Association), Eighth Session, Melbourne, August, 1952.

Periarticular œdema subsides and most of the tissues return to normal. Lengthened or shortened muscles resume their correct length, and the balance of muscles is restored. The deforming and ankylosing process is the end-result of a pathological state which should not have been allowed to persist. Ankylosis will occur in any damaged joint if it is damaged afresh every day.

Continuous versus Intermittent Immobilization.

The usual reply to the problem of continuous *versus* intermittent immobilization is that it is not new—that everyone practises splinting of rheumatoid joints. That is true; but not continuous splinting. I am well aware that intermittent splinting is advised by general agreement, and I am aware that it is practised by some. Intermittent splinting—a caliper for the knee of a walking patient or a posterior cast for use in bed, for the wrist a removable cast—is commonly used, and it is extremely valuable in the treatment of suitable patients. But if intermittent splinting is valuable, in most cases continuous splinting is still more valuable. The patient is asking you to treat his painful and swollen joint, and we should apply the measures most effective to this end. In a painful and swollen joint, when a splint has been applied, a daily movement undoes much of the good that the splinting has done.

There is a world of difference between continuous and intermittent immobilization for acutely painful joints. If the joint needs rest, it needs a lot of rest, until the object of treatment—abatement of pain and swelling—is achieved.

I do not wish to be misunderstood. I am not decrying intermittent splinting. For acutely painful joints it is better than no splinting at all. And as a long-term measure in the treatment of damaged—but not acutely painful and swollen—joints it is the great stand-by for the prevention of deformity. I use intermittent splinting as a routine in the following circumstances: (i) for a few weeks, the gradual restoration of movements when continuous splinting has come to an end; (ii) for a prolonged period, to support weakened muscles and prevent deformity; (iii) to assist active movements of fingers by supporting metacarpo-phalangeal joints in extension.

Active Use of Limb.

The principle I stated earlier declares that as far as is technically possible and consistent with use of the limb, inflamed joints should be immobilized continuously.

Treatment of rheumatoid arthritis should aim at keeping the patient out of bed, moving his limbs and contracting his muscles. If, while a joint is immobilized, the muscles are allowed to waste away through inactivity, the treatment is worse than useless. Therefore the joints which are not immobilized should be actively used. The general orthopædic principle of immobilizing neighbouring joints is disobeyed; if these joints are healthy they must be actively used. While the knee is immobilized the limb must be used for weight-bearing, and quadriceps drill must be continuous. When the ankle or the joints of the foot are in a plaster splint the patient must walk. If only tarsal or metatarsal joints are inflamed, it is usually possible to leave the ankle out of the plaster splint. While the elbow or the wrist is immobilized, the fingers and the shoulder should be actively used. While the metacarpo-phalangeal joints are fixed, the interphalangeal joints must be actively used. Digital tendons must be kept moving—not allowed to become adherent to their sheaths as they cross the inflamed joints.

Technique.

I have treated successfully by this method every joint except the hip and the joints of the vertebral column. Swaim (1939) insists that the spread of *spondylitis ankylopoietica* may be arrested by a plaster jacket. I have not succeeded; I do not believe that movements between adjacent articular processes can be sufficiently controlled by a jacket. Fortunately the hip—which is very difficult to treat—is less commonly involved than any other joint.

The Knee.

In inflamed joints the chief stimulus to pain is movement, not pressure. A painful knee becomes painless as soon as it is immobile; the patient may walk without pain on a straight limb which has been fixed in plaster, or in a caliper which does not take the body-weight off the limb (Figure I). Weight-bearing is good for the limb, and

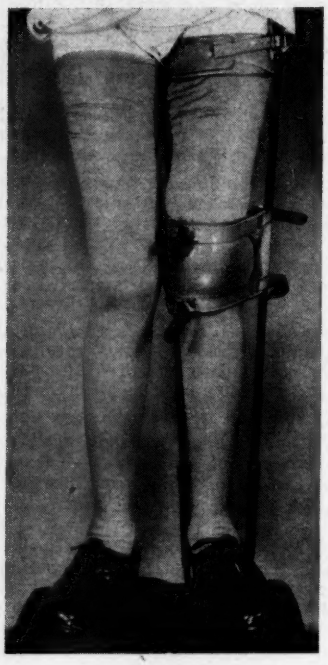

FIGURE I.

Band caliper which keeps knee extended and allows limb to bear weight.

quadriceps drill must be unceasing. After removal of the splint a caliper or a posterior splint should be worn intermittently and flexion gradually restored. In arthritis of the knee the danger to be guarded against is a flexion deformity. Predisposing to flexion we have several factors: body weight, wasting of the quadriceps, spasm of the flexors, habitual flexion when sitting or lying on the side, relative comfort of the flexed position, disinclination to walk. To overcome these the quadriceps must be supported and strengthened.

The Ankle.

The ankle should be immobilized in a plaster cast with a walking iron. So far I have found the treatment less successful than that of other joints, and I am coming to believe that weight-bearing should be disallowed. This is difficult when both ankles are involved.

Tarsal and Metatarsal Joints.

When the ankle is not involved, diseased tarsal joints can be immobilized by applying a plaster slipper which leaves the ankle free (Figure II). If the metatarsal joints alone are involved and the tarsal joints have escaped, a plaster splint which encircles only the front half of the foot is sufficient (Figure III). Here again we meet with illustrations of the principle that the chief stimulus to pain is movement, not pressure. When metatarsal joints have been so painful that the patient cannot put his foot to the ground, immediately after application of the plaster he can stamp his foot without pain. Bearing weight on the joints is not painful if movement of the articular surfaces is avoided.

The Shoulder.

A painful and stiff shoulder should be immobilized, if immobilization is necessary, in the fashion Nature intended —by binding of the humerus to the chest wall. The forearm is supported in a sling and the hand and wrist are used. The pain ceases immediately; the more complete the fixation, the more rapidly will the inflammatory reaction subside. Then the range may be restored by active movements. Paradoxically, fixation of the humerus to the chest wall does not induce a stiff and frozen shoulder; it prevents it.

FIGURE II.

Plaster slippers to immobilize joints of feet and leave ankles free.

FIGURE III.

Plaster applied to all four extremities, including metatarsophalangeal joints. Remission resulted, of six months' duration.

The Elbow.

A painful and swollen elbow should be fixed at right angles, with the forearm midway between pronation and supination. The plaster splint should extend to the axillary fold and nearly to the wrist; wrist and fingers, if not involved, should be left free and actively used. On removal of the plaster a sling should be worn for a few weeks and restoration of movements should be gradual (Figures IVA, IVB).

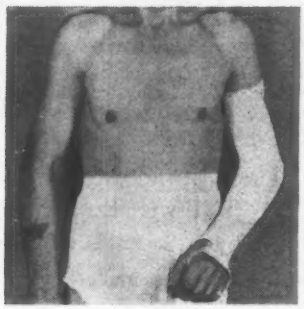

FIGURE IVA.

Splint applied at 90° for effusion of left elbow.

The Wrist.

The wrist is one of the key joints. When it has been painful, immobile and flexed for a few weeks, irreparable harm will have been done. The hand will be painful and motionless, and the arm will be held to the side; thus the scapulo-humeral joint may become fixed. All this can be avoided if the wrist is fixed in slight extension and the hand is freely used. The fingers and thumb are quite free, and rotary movements of the forearm should be unhampered; this can be achieved if the plaster splint is applied with the forearm midway between pronation and supination. After four or five weeks of fixation a plaster splint or a leather support should be worn intermittently for gradually diminishing intervals (Kelly, 1950).

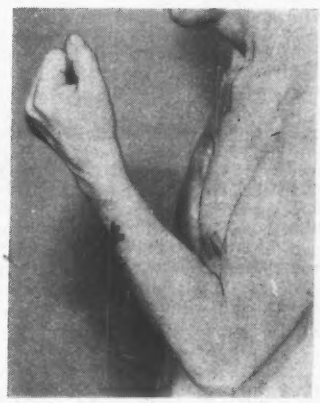

FIGURE IVB.

Range of flexion of left elbow two months after removal of plaster.

The Metacarpo-Phalangeal (Basal) Joints.

The metacarpo-phalangeal joints are among the key joints (the others are the knee and the wrist). When the basal joints are painful and swollen, the flexor sheaths become œdematous where they cross the joints; the tendons do not slide well and the interphalangeal joints cannot be flexed. The patient can grasp only with straight fingers, hyperflexed at the basal joints, and he practises indiscriminate exercises, which further irritate the inflamed

surfaces. The basal joints later become subluxated, and ulnar deviation follows if the joint of the little finger is involved. This deformity can be prevented, and the function of the hand can be preserved, if the basal joints are fixed in extension, the interphalangeal joints left free, and the hand is used as much as possible. Afterwards a removable splint is used, which may be slipped on and off. When the basal joints are fixed, exercises to flex the middle and terminal joints are more effective (Kelly, 1950).

Individual basal or interphalangeal joints may cause severe pain. Dramatic relief may be obtained by splinting them continuously or intermittently, and leaving all the other joints free.

Which Joints to Immobilize.

When a patient comes with half a dozen or more painful and swollen joints, we have to decide which ones to immobilize. The key joints (knees, hands and wrists) must be watched, because irreparable damage may follow a few weeks' neglect of any of them. Involvement of the hips is not common and involvement of the spine (ankylosing spondylitis) does not lead to permanent crippling; neither does damage to the feet, ankles, elbows or shoulders. But damage to knees, wrists or hands may lead to permanent crippling.

The painful swollen hand should be carefully examined by palpation to decide whether the wrist or the metacarpophalangeal joints are more severely involved. Acute tenderness on the volar aspect of the joint may be the only deciding factor (Figure V). If both are equally painful, the wrist (B) should be immobilized; for then the basal joints (A) may improve. If they do not, the plaster splint should be extended to immobilize them. The basal joints should be freed again after two weeks, and the wrist kept fixed for a further three weeks. If both wrists or both hands are painful and swollen, they should be immobilized at the same time. If one knee or one or both feet require treatment they should be treated too. I have frequently put plaster splints on all four extremities and allowed the patient to go home (Figure III). I have immobilized both knees together, but not at the same time as the feet or the hands. It is harder to render the ankle free from pain than any other joint. If one joint is acutely painful and a number of others are only slightly so, the one joint should be immobilized, in the hope that the pain in the others will subside—which frequently happens. So frequently have I seen pain and stiffness disappear from the shoulder after immobilization of the wrist, that I have come to regard it as a normal result. Pain in the feet often disappears after immobilization of the hands, and a small effusion in one knee will often subside when its more severely involved fellow is immobilized.

Results.

The main symptom of rheumatoid arthritis is pain. Exhaustion and ill-health are caused by the multiple inflammatory foci, and intensified by the intractable pain, the sleeplessness and the anxiety. The effect of immobilization of the painful and swollen joints is to relieve the pain and abolish the multiple foci. It is not surprising, therefore, that the patient feels much better within a few hours of the immobilization of the most painful joints.

Rheumatoid arthritis, it has been recognized for years, is always potentially reversible. This applies not only to the disorder as a whole, but to each individual joint; even the most inflamed and apparently disorganized joint may take a sudden turn and resume a normal appearance. Treatment by immobilization, therefore, is rational in that it makes actual a capacity which always is potential. Moreover, we should not be surprised that a general remission may follow the application of a plaster splint to the most severely involved joints; we would rather expect it.

When I have tried to describe the effects of treatment with plaster of Paris, the reply often has been "but of course it always recurs". But it does not always occur. It usually recurs eventually in the same patient, but not always in the same joints. I could give dozens of instances of joints which were immobilized more than four years ago, and which have never been painful since, though other joints in the same patient have been painful. If the same joints become involved again, the same treatment may be applied again, at little inconvenience to the patient.

In rheumatoid arthritis each individual joint calls for treatment, and the principles do not differ from the principles of treatment of any other articular disease. But the method of their application is different, for the following reasons: (i) a large number of joints may be involved; (ii) the inflammation tends to recur; (iii) there is a danger of deformity and ankylosis. However, none of these difficulties is insurmountable.

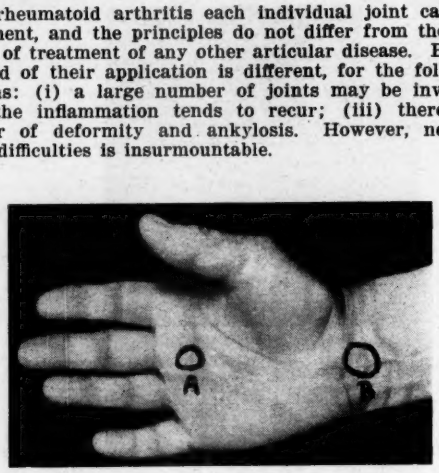

FIGURE V.

A, site of acute tenderness in arthritis of basal joints of middle finger. B, site of acute tenderness in arthritis of wrist.

Historical Survey.

The question of continuous splinting for rheumatoid arthritis has cropped up from time to time in the literature, but it has always been haunted by the shadow of ankylosis, and active use of the limb has not been insisted on. Our profession has a traditional bias in favour of movement in the treatment of joint diseases, though at intervals John Hunter (1835), John Hilton (1863) and Hugh Owen Thomas (1878) have arisen to stress the value of rest. Thomas, a general practitioner who came from a long line of manipulators, was so appalled by the dreadful results of passive movements that he fixed all diseased joints for long periods. He achieved unprecedented results with his methods; but his fame was somewhat diminished by his scornful criticisms of those he disagreed with. Thomas wrote as follows:

> It matters not from what cause these affections arise, whether from an injury, rheumatic attack or constitutional defect, the main thing needful, especially in the chronic stage, is that the joint be mechanically fixed, the general health being attended to if necessary.

Nobody had yet learned to differentiate tuberculosis from other joint diseases; when this differentiation was made, absolute fixation was applied only to tuberculous joints. But Thomas's nephew, Robert Jones (1909), insisted on the value of fixation in chronic non-tuberculous arthritis:

> Clinical evidence is overwhelming that friction of the joint surfaces in the hypertrophic form of arthritis is a factor to be scrupulously avoided. Any treatment which ignores this is faulty.

Phelps (1890) carried on a campaign in America against movement of painful joints. He proved in dogs that no ankylosis resulted after fixation for five months. This was but confirming the work of Reyher (1874), who made histological studies of the articular cartilage; it was confirmed more recently by Ely and Mensor (1933). Phelps wrote as follows:

> Our text-books on surgery are filled with notes warning against prolonged immobilization in the treatment of inflamed joints, lest ankylosis result. . . . Motion of an inflamed joint only interferes with repair, and more certainly hastens the case on to ankylosis and deformity.

More recently, Vincent Coates (1933), of Bath, came to see the value of immobilization of joints, and after his death Kindersley (1935, 1938) described the methods he used. Kindersley would not carry on immobilization for longer than two weeks, and he seemed somewhat over-anxious to hurry the return of movements. Moreover, he kept his knee patients in bed, and did not insist at all on the active use of the limb. Yet he undoubtedly secured valuable results.

The principle of rest for chronic rheumatic joints is admitted on all sides, yet it is not put into practice. Pemberton (1945) conducted a survey of American physicians and found that only 11% use rest as a routine measure. Perhaps the reason is that the method generally recommended (intermittent splinting) does not give adequate results. In the literature of rheumatism in the past twenty years, many writers can be found who stress the supreme importance of splinting the joints; yet the splinting recommended by all except Kindersley and three others was intermittent only. The other exceptions are as follows: (i) Tippett (1940), who would not hesitate to keep joints immobilized for a month. (ii) Bell (1940), who wrote: "The fear is often expressed that immobilization will result in a stiff joint. Movement in an inflamed joint is much more likely to result in a stiff joint, as movement aggravates the inflammatory process." (iii) Aitken (1935), who wrote in the following terms:

> Any movement of an inflamed joint will tend to produce ankylosis and to undo the possibility of recovery with movement. This rule has not been accepted or practised by those who deal with chronic arthritic joints in various rheumatic types of arthritis which cripple so many adults, and until this is accepted very little progress in the prevention of deformity will be made in this branch of therapeutics.

Summary.

1. In rheumatoid arthritis the most crippling deformities are those affecting the hands, wrists and knees; if these can be prevented the patient will be able to lead a useful life.

2. Deformity and ankylosis are the end-results of a pathological condition which is perpetuated and intensified by repeated movements.

3. When joints are acutely painful and swollen, continuous immobilization in plaster of Paris for three to five weeks relieves the pain immediately and causes the swelling to subside.

4. The joints are splinted so as to allow use of the limb and movements of the unaffected joints, and active contraction of the muscles is practised continuously. Rest in bed is not recommended.

5. On removal of the plaster splint the involved joints are splinted intermittently, and restoration of movements is gradual. There is no danger of ankylosis.

6. A number of joints may be immobilized at once, with a remarkable improvement in the patient's general health.

7. The principle of continuous immobilization is in conformity with traditional orthopædic principles.

References.

AITKEN, D. M. (1935), "Hugh Owen Thomas. His Principles and Practice", London.

BELL, B. T. (1940), "The Prevention and Correction of Deformities in Arthritis", *M. Clin. North America*, 24 : 1735.

COATES, V. (1933), "Modern Methods in the Treatment of Chronic Arthritis", *Practitioner*, 131 : 454.

ELY, L. W., and MENSOR, M. C. (1933), "Studies on the Immobilization of the Normal Joints", *Surg., Gynec. & Obst.*, 57 : 212.

HILTON, J. (1863), "Lectures on Rest and Pain", London.

HUNTER, J. (1835), "The Works of John Hunter, F.R.S.", London.

JONES, R. (1909), "Surgical Treatment of the Rheumatoid Group of Affections", *Brit. M. J.*, 1 : 2.

KELLY, M. (1950), "The Prevention of Deformity in Rheumatic Disease", M. J. AUSTRALIA, 2 : 1.

KINDERSLEY, C. E. (1935), "Discussion on the Immobilization Treatment of Arthritis", *Proc. Roy. Soc. Med.*, 29 : 237.

KINDERSLEY, C. E. (1938), "The Use of Plaster Splints in Arthritis", *J. Roy. Inst. Pub. Health & Hyg.*, 1 : 400.

PEMBERTON, R. (1945), "Recent Developments in Chronic Arthritis", *Am. J. M. Sc.*, 209 : 364.

PHELPS, A. M. (1890), "The Question of What Produces and What Prevents Ankylosis of Joints", *New York M. J.*, 51 : 536.

REYHER, C. (1874), "On the Cartilages and Synovial Membranes of Joints", *J. Anat. & Physiol.*, 8 : 261.

SWAIM, L. T. (1939), "The Orthopedic Treatment of Strümpell-Marie Arthritis", *J. Bone & Joint Surg.*, 21 : 983.

THOMAS, H. O. (1878), "Diseases of the Hip, Knee and Ankle-Joints, and Their Treatment by a New and Efficient Method", Liverpool.

TIPPETT, G. O. (1940), "The Use of Plaster Splinting in the Treatment of Arthritis", *Brit. J. Rheumat.*, 2 : 195.

Reports of Cases.

GRANULOSA CELL TUMOUR OF THE OVARY WITH SPREAD TO ENDOMETRIUM AND CERVIX.

By A. R. H. DUGGAN,
Sydney.

GRANULOSA cell tumours of the ovary are not common, and it would appear from recent writings that they are more malignant than was formerly thought. Unusual forms and complications add to our knowledge of these tumours, and as I cannot find any evidence in the available literature of granulosa cell tumour appearing in the endometrium and cervix, this case is reported.

The relevant history of the patient is as follows.

Mrs. T., aged forty-four years, was a nulliparous widow. From the age of twenty-nine to forty-three years her menstrual periods were scanty and irregular, and she had intervals of several months of amenorrhœa. In July, 1952, she noticed a mucopurulent discharge, which ceased after sulphonamide therapy and was followed by a serosanguineous discharge and occasional vaginal "spotting" of bright blood. One month prior to her admission to hospital she endured three weeks of continuous and sometimes excessive blood loss. She had no abdominal pain, had lost no weight, and had some discomfort on defæcation and some frequency of micturition for six weeks. There was nothing else relevant in her history. She had not been pregnant.

On examination of the patient, the general systems were normal. Bimanual examination revealed the uterus to be anterior, of normal size and shape and firm, the mobility being slightly restricted, with some tenderness on the right side. There appeared to be a small polypus at the external os. The right appendage was normal, the left ovary was enlarged to the size of a golf ball, firm and not tender.

At operation the patient was placed in the lithotomy position, and on dilatation of the *os cervicis* small pieces of soft friable tissue came away. Curettage removed large quantities of this material. A tentative diagnosis of adenocarcinoma of the uterus with metastases in the left ovary was made. Examination on section revealed a uterus of normal size and an enlarged round left ovary, about two inches in diameter, which broke into irregular fragments when lifted out of the pelvis. There was a nodule about half an inch in diameter on the right side of the uterus under the upper edge of the bladder. The right ovary appeared normal. The uterus was of normal size, but somewhat softer than usual. Total hysterectomy and double salpingo-oophorectomy were performed. The uterus was opened, and large fungating friable masses were found filling the cavity of the uterus and the cervix.

Microscopic examination revealed cystic hyperplasia of the endometrium invaded by typical follicular type granulosa cell carcinoma. There were granulosa cell deposits in the myometrium as well, and in the cervical tissue

(Figures I and II). In the left ovary and the uterine nodule under the bladder follicular granulosa cell carcinoma was found. No metastatic deposits were found in the Fallopian tubes or the right ovary (Figure III).

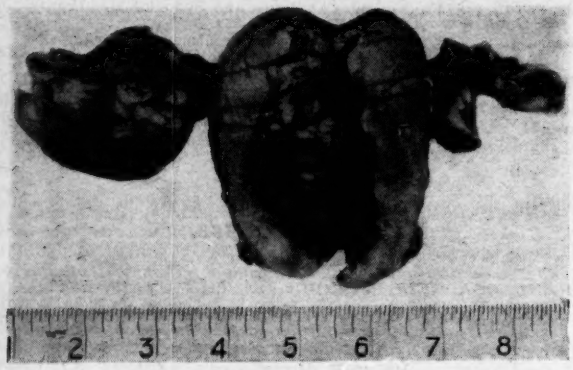

FIGURE III.
Macroscopic appearance of specimen, showing fungating friable masses in the uterine and cervical cavity, and tumour of the left ovary.

The value of deep X-ray therapy following operation in this condition has been questioned. Recurrent granulosa cell carcinoma has been found many years after the original operation.

Legends to Illustrations.

FIGURE I.—Granulosa cell carcinoma in the ovary.

FIGURE II.—Granulosa cell masses invading cystic hyperplastic endometrium and myometrium.

APLASTIC CRISIS IN CONGENITAL HÆMOLYTIC ICTERUS (ACHOLURIC JAUNDICE): A DESCRIPTION OF THREE CASES.

By J. MARGOLIS.

From the Department of Pathology, Royal Alexandra Hospital for Children, Sydney.

THE pathogenesis of the acute crisis in congenital hæmolytic icterus has not been questioned until recent years, and the phenomenon was considered to be a sudden increase in the rapidity of red cell destruction; hence the term "hæmolytic crisis" is uniformly found in the standard texts. With the advent of accurate methods of estimating the erythrocyte survival time, a much clearer picture of the fate of the red cells in hæmolytic disorders has been formed. Whilst it is still uncertain what constitutes the basic defect in the cell ultrastructure, it can be accepted that the life span of the erythrocytes in congenital acholuric jaundice is approximately one-tenth of normal, and it follows that the bone marrow must produce a corresponding number of new cells if the normal blood level is to be maintained. Should an even transient failure of the marrow occur, a rapid development of severe anæmia is to be expected without the need to postulate any increase in hæmolysis above that already present.

Owren in 1949 described six cases of acute crisis in which the blood findings pointed to an aplasia of erythropoietic elements as the cause of the acute onset of anæmia. His attention was directed to the uniformly low reticulocyte and serum bilirubin levels at the height of the anæmia, and whilst similar observations had been made in the past by other authors, on this occasion the aplastic state was actually demonstrated on the fourth and the sixth days after the onset of symptoms in the one case in which the opportunity of marrow biopsy at the critical stage presented itself. The author suggested that the use of the term "hæmolytic crisis" be discontinued and the term "aplastic crisis" substituted for it.

Damashek and Bloom (1948) analysed the data of seven cases of acute crisis, and whilst confirming the presence of low reticulocyte counts and serum bilirubin levels, they were not able to demonstrate an aplastic state in the bone marrow. The acute anæmia was attributed to maturation arrest of erythropoietic elements, as a result of inhibitory splenic action. This interpretation is open to the criticism that the marrow examinations were not performed at the critical stage and the aplastic phase could thus have been missed.

The following cases of acute crisis occurring at short intervals in three members of one family are of interest, not so much because such incidents are relatively uncommon, but because they afford an opportunity to collect some data, which, although not complete in each individual case, when correlated appear to fit into a definite pattern clearly pointing to aplastic basis of the anæmia. The bone marrow in Case I was examined in the aplastic stage, and a few days afterwards. The hæmoglobin levels in Cases II and III were determined and found to be normal immediately prior to the onset of symptoms, but unfortunately these two children were prevented from returning to the laboratory for further investigation by an illness which was only later realized to be the onset of acute crisis.

The three patients were the only siblings in a family affected by acholuric jaundice on the mother's side. The maternal grandfather had a history of splenomegaly and jaundice; a maternal aunt suffered from anæmia which was cured by splenectomy, although spherocytes were stated to be still present in her blood after the operation. Although the mother herself had no definite history of anæmia, examination of her blood at this laboratory revealed a pronounced degree of spherocytosis, a reticulocyte count of 15% in spite of a relatively normal hæmoglobin value (12·8 grammes *per centum*) and considerably increased osmotic fragility, which was quantitatively estimated in fresh defibrinated blood and in blood incubated at 37° C. for twenty-four hours. No abnormality could be detected in the father's blood.

Case I.

T.S., a boy, aged six years, was admitted to the hospital on September 2, 1952, with severe anæmia. He was stated to be usually of good health, except for attacks of tonsillitis which were often treated with sulphonamides. Six weeks previously he had suffered from gastro-enteritis, for which he was also given sulphonamide tablets. After that incident he remained in his usual state of health until August 29, when he complained of tiredness and pallor was noted. On the following day he vomited repeatedly and complained of upper abdominal pain and headache. The pallor and malaise continued to increase during the following two days, and on September 1 he had an epistaxis which was still present on his admission to the hospital.

On examination he was extremely pale and very weak and dyspnœic. Physical examination revealed a rapid heart rate, a systolic murmur maximum in the pulmonary area, a palpable spleen and bright red blood in the nasopharynx. There was no obvious jaundice and no other abnormalities were detected. A provisional diagnosis of acute leuchæmia was suggested, and a blood count was immediately performed with the following result: the hæmoglobin value was 3·6 grammes *per centum*, and the red cells numbered 1,050,000 per cubic millimetre. The leucocytes numbered 5000 per cubic millimetre, 74% being neutrophile cells, 24% lymphocytes and 2% monocytes. Platelets appeared to be present in normal numbers. The erythrocytes were affected by a moderate degree of spherocytosis, and no nucleated forms were seen. The response to the direct Coombs test was negative.

A transfusion of 500 millilitres of whole blood was given, and the patient made an uninterrupted recovery and was discharged from hospital on September 13. Two iliac crest

TABLE I.

Case 1 (T.S.).

Date.	Hæmoglobin Value. (Grammes *per Centum.*)	Erythrocytes per Cubic Millimetre.	Reticulocytes.	Bone Marrow Findings.	Other Findings and Remarks.
29. 8.52					Onset of present symptoms.
2. 9.52	3·6	1,050,000	—		Coombs test result negative. Blood transfusion.
3. 9.52	7·0			Iliac crest marrow: Myeloblasts .. .. 1·0%; Promyelocytes .. 1·5%; Myelocytes .. .. 11·0%; Metamyelocytes .. 21·0%; Polymorphs .. .. 15·0%; Eosinophile cells .. 2·5%; Basophile cells .. 1·0%; Lymphocytes .. .. 39·0%; Monocytes .. .. 1·0%; Plasma cells .. .. 1·5%; Proerythroblasts .. 0·5%; Normoblasts .. .. 5·0%. (Majority basophilic and stunted forms.)	Urinary urobilinogen content increased.
5. 9.52	8·8	2,870,000	0·5%		Serum bilirubin content 0·9 milligramme *per centum*. Urinary urobilinogen content increased.
8. 9.52	9·5	3,320,000	0·5%		
10. 9.52	11·4	3,440,000	5·0%	Iliac crest marrow: Myeloblasts .. .. 1·0%; Promyelocytes .. 1·5%; Myelocytes .. .. 11·0%; Metamyelocytes .. 18·0%; Polymorphs .. .. 17·0%; Eosinophile cells .. 4·0%; Basophile cells .. — ; Lymphocytes .. .. 9·0%; Monocytes .. .. 0·5%; Plasma cells .. .. 0·5%; Early normoblasts .. 1·5%; Intermediate normoblasts .. .. .. 13·0%; Late normoblasts .. 23·0%	
25. 9.52	11·0		6·0%		Osmotic fragility: hæmolysis commences at 0·62% sodium chloride solution; hæmolysis 50% at 0·48% sodium chloride solution; hæmolysis complete at 0·28% sodium chloride solution.
4.11.52	10·0	3,370,000	12·0%		

marrow punctures were performed. Examination of the marrow obtained at the first puncture, on September 3, revealed a gross depression of red cell precursors, which comprised only 5% of the nucleated cells, the majority being somewhat atypical in appearance with blurred nuclear pattern, which made it often very difficult to identify these cells as such. Only a very occasional orthochromatic normoblast could be found, the majority of the cells being deeply basophilic. Examination of marrow obtained at the second aspiration biopsy of the opposite iliac crest six days later revealed it to be active normoblastic marrow with 37·5% normally maturing erythrocyte precursors. The details of relevant investigations are shown in Table I.

Case II.

P.S., a girl, aged eight years, sister of T.S., was admitted to the hospital on September 13, 1952, with the following history. After an attack of gastro-enteritis three years previously she had made a very slow recovery and was noticed to be pale. A blood examination on that occasion revealed "fragile red cells". After this incident she had remained well until September 4, 1952, when she vomited in the evening. The nausea persisted and the next day was accompanied by abdominal pain and later by irregular fever. On September 6 pallor and lassitude were noted, and these continued to increase until her admission to hospital. A course of sulphaguanidine was commenced on September 6. Throughout her illness she remained constipated. The urine was stated to be cloudy, but of normal colour.

A blood examination was performed in the course of investigation of her brother's symptoms on September 4, the day of onset of her illness. The hæmoglobin value was then 12·3 grammes *per centum* and numerous spherocytes were seen in the stained blood films.

On her admission to hospital she was in a very similar condition to that of her brother (Case I) eleven days previously. She was very pale and weak, and had a palpable spleen and a hæmic heart murmur. No hæmorrhagic manifestations were present, and no jaundice was seen. A blood count on her admission to hospital gave the following information: the hæmoglobin value was 3·8 grammes *per centum*; the red cells numbered 1,480,000 per cubic millimetre, reticulocytes being less than 1% and nucleated red cells 4600 per cubic millimetre; the leucocytes numbered 20,000 per cubic millimetre, 77% being neutrophile cells, 20% lymphocytes, 2% monocytes and 1% eosinophile cells. Thrombocytes were present in normal numbers. The response to the direct Coombs test was negative. After a transfusion of 500 millilitres of whole blood she made an uninterrupted recovery and was discharged from hospital on September 25. Examination of marrow aspirated from the iliac crest on September 14 revealed it to be highly cellular marrow with 78% nucleated red cells, only a very small proportion of which, however, were orthochromatic, the majority being basophilic. The details of investigations are given in Table II.

Case III.

W.S., aged four years, sister of the other two children, was admitted to hospital on September 13, 1952, together with her elder sister (Case II), with a practically identical history in regard to both symptoms and the time of onset. She was stated six months and eighteen months previously to have had attacks of rheumatic fever, but the description of symptoms on those occasions was rather inconclusive. In early infancy she had been given three blood transfusions for anæmia, thought to be due to hæmolytic disease of the new-born, the patient being Rh-positive and her mother Rh-negative. On September 4, immediately prior to the onset of the present illness, her hæmoglobin value was 11·2 grammes *per centum*, and numerous spherocytes were seen on examination of stained films. On her admission to hospital, in addition to extreme pallor

and a palpable spleen, as seen in the previous two cases, she had a harsh systolic murmur maximal at the mitral area, and the heart appeared to be clinically enlarged, although subsequent radiographs of the chest showed its size to be within normal limits. A blood count revealed that the hæmoglobin value was 3·6 grammes *per centum*, the red cells numbered 1,560,000 per cubic millimetre, reticulocytes being less than 0·5%, and nucleated erythrocytes 1000 per cubic millimetre; the leucocytes numbered 10,000 per cubic millimetre, of which 82% were neutrophile cells, 16% lymphocytes and 2% monocytes. The response to the direct Coombs test was negative.

After a transfusion of 500 millilitres of whole blood the patient made an uneventful recovery and was discharged from hospital on September 29. An iliac crest puncture on September 14 yielded highly cellular marrow containing 77% nucleated red cells, only a very occasional one of which was orthochromatic. Other findings are set out in Table III.

In view of the history of suspected Rh incompatibility, the mother's blood was sent to the Red Cross Blood Transfusion Service laboratory for antibody studies, and the report was received that only very weak untitrable antibodies were detected by an indirect antiglobulin test.

Discussion.

The illness in all three cases followed a similar pattern, both in the time relations and in the blood findings. In Case I, aplasia of erythropoietic elements of bone marrow was found on the sixth day after the onset of definite symptoms, and it must have been followed by rapid regeneration, since active normoblastic marrow with normal maturation of the red cell precursors was demonstrated six days later. In the other two cases the earliest change demonstrated was an early stage of very active normoblastic hyperplasia. Since, however, these patients' admission to the hospital was relatively later, it is highly probable that an aplastic picture could have been present some four days earlier. As it is, the appearance of the two bone marrows corresponded to the "maturation arrest" described by Damashek and Bloom; but it is apparent that this state, in all probability, represented a transition stage between aplastic and normally matured bone marrow.

Although the opportunity was not afforded to study the history of these two patients between the time when their hæmoglobin values were normal and nine days later, when approximately 75% of their red cells had disappeared from the circulation, such changes are consistent with a sudden cessation of bone marrow activity, if the abnormally short life span of the erythrocytes is remembered.

The presence of nucleated red cells in peripheral blood coincident with a low reticulocyte level suggests a response to severe anæmia of bone marrow in which the vast majority of red cell precursors were still in the early stages of maturation, and only a very few had advanced to the stage of reticulocytes. In Case I the anæmia was corrected by blood transfusion whilst the marrow was still in the aplastic stage, and such a response could not, therefore, have been expected.

The history of neonatal anæmia in W.S. (Case III) deserves a comment. Since no significant level of antibodies could be detected in the mother's blood, it is very unlikely that the anæmia was due to Rh incompatibility, and much more likely that it was a manifestation of congenital acholuric jaundice.

A composite picture which emerges from the description of the three cases appears to be a sudden cessation of erythropoiesis precipitated by some external disturbance, most probably an infection, which is followed shortly after by disappearance of the majority of red cell precursors from the bone marrow. On the seventh or eighth day rapid regeneration takes place; but the normoblasts are not fully mature until the twelfth day, when an increase in reticulocytes takes places. This sequence of events is almost identical with that reported by Owren.

The effect of blood transfusions on the resumption of bone marrow activity must remain doubtful; but since in a number of similar reported cases blood transfusion was not given, and recovery still occurred at a similar time interval, it is probable that transfusions had no specific effect apart from tiding the patients over the danger period.

The paucity of cases in the literature in which aplasia of erythropoietic elements can be actually demonstrated may be due to the difficulty of obtaining a specimen of rapidly changing marrow at the critical stage, as these cases are most likely to be investigated when the aplastic phase is over, which is what has probably happened in Cases II and III described above.

The fact that crisis is almost unknown after splenectomy does not necessarily implicate the spleen as its causation, since the life span of spherocytes becomes practically

TABLE II.

Case II (P.S.).

Date.	Hæmoglobin Value. (Grammes *per Centum*.)	Erythrocytes per Cubic Millimetre.	Reticulocytes.	Bone Marrow.	Other Findings and Remarks.
4. 9.52	12·3	—	—	—	Onset of present symptoms.
13. 9.52	3·8	1,480,000	Less than 1·0%		Coombs test result negative. Nucleated red cells 4600 per cubic millimetre. Blood transfusion.
14. 9.52	—	—	—	Iliac crest marrow:	
15. 9.52	8·4	3,140,000	2·2%	Myeloblasts .. .. 0·5% Promyelocytes .. 1·5% Myelocytes .. .. 5·0% Metamyelocytes .. 5·0% Polymorphs .. .. 5·0% Eosinophile cells .. 1·5% Basophile cells .. — Lymphocytes .. .. 3·0% Monocytes .. .. 0·5% Proerythroblasts .. 1·0% Early normoblasts .. 23·0% Intermediate normoblasts .. .. .. 38·0% Late polychromatic normoblasts .. 14·0% Late orthochromatic normoblasts .. 2·0%	Occasional nucleated red cells. Serum bilirubin 0·7 milligramme *per centum*.
17. 9.52	10·0	3,610,000	8·0%		Urinary urobilinogen content slightly increased. Nucleated red cells absent.
18. 9.52	—	—	—		Osmotic fragility: hæmolysis commenced at 0·64% sodium chloride solution; hæmolysis 50% at 0·44% sodium chloride solution; hæmolysis complete at 0·28% sodium chloride solution.
19. 9.52	9·5	3,580,000	8·0%		
24. 9.52	9·9	3,430,000	6·0%		Serum bilirubin content 0·6 milligramme *per centum*.
4.11.52	11·4	4,080,000	10·0%		

TABLE III.
Case III (W.S.)

Date.	*Hæmoglobin* Value. (Grammes *per Centum.*)	Erythrocytes per Cubic Millimetre.	Reticulocytes.	Bone Marrow.	Other Findings and Remarks.
4. 9.52	11·2	—	—	—	Spherocytosis present.
5. 9.52	—	—	—	—	Onset of present symptoms.
13. 9.52	3·6	1,560,000	Less than 0·5%	—	Nucleated red cells 1000 per cubic millimetre. Coombs test result negative. Blood transfusion.
14. 9.52	—	—	—	Iliac crest marrow: Myeloblasts .. .. 0·5% Promyelocytes .. 0·5% Myelocytes .. .. 7·0% *Metamyelocytes* .. 5·0% Polymorphs .. .. 5·0% Eosinophile cells .. 2·5% Basophile cells .. — Lymphocytes .. .. 2·0% Monocytes .. .. 0·5% Proerythroblasts .. 2·0% Early normoblasts .. 22·0% Intermediate normoblasts .. .. 47·0% Late normoblasts .. 6·0% (Only very occasional orthochromatic normoblasts were seen.)	Serum bilirubin content less than 0·5 milligramme *per centum.* Urinary urobilinogen content moderately increased.
17. 9.52	10·1	3,900,000	4·6%		—
18. 9.52	—	—	—		Osmotic fragility: hæmolysis commenced at 0·60% sodium chloride solution; hæmolysis 50% at 0·40% sodium chloride solution; hæmolysis complete at 0·28% sodium chloride sloution.
19. 9.52	10·3	3,950,000	5·1%		Urinary urobilinogen content moderately increased.
24. 9.52	10·7	—	3·0%		Serum bilirubin content 0·5 milligramme *per centum.*
4.11.52	10·0	3,500,000	13·0%	—	—

normal after this operation (Schrumpf, 1950, quoted by Crosby), and temporary marrow aplasia could not be expected to result in anything like the grave anæmia encountered in non-splenectomized patients, but only in a slight drop in hæmoglobin value, which need not be detected clinically. Indeed, it makes one wonder whether the agent or agents that are responsible for acute crisis in our patients may not have a similar effect on the marrow of normal persons. What the nature of such agents is has not been as yet conclusively shown, although indirect evidence points to an infection, possibly of virus origin (Dedichen, 1947; Horne *et alii*, 1945). This hypothesis is suggested not only by the frequent occurrence of crisis in several members of a family, with a few days' "incubation period" in between, but also by an occasional simultaneous febrile illness of other contacts not affected by acholuric jaundice. It would be tempting to speculate on the changes in the bone marrow of such contacts, although for obvious reasons the opportunity to confirm these suspicions must remain rather remote.

Summary.

Recent views on the nature of "hæmolytic crisis" in congenital acholuric jaundice are briefly reviewed. Three cases of such crisis occurring in the same family at short intervals are described; in one, the marrow aplasia was demonstrated; in the two others it was presumed to have been present several days prior to the marrow biopsy.

Acknowledgements.

I wish to express my gratitude to Dr. D. Vickery for his permission to publish these cases, to Dr. R. D. K. Reye for the criticism of this report, and to Dr. H. M. Learoyd and the members of the laboratory staff of the Royal Alexandra Hospital for Children for their assistance with laboratory investigations.

References.

CROSBY, W. (1952), "The Pathogenesis of Spherocytes and Leptocytes (Target Cells)", *Blood*, 7: 261.

DAMASHEK, W., and BLOOM, M. L. (1948), "The Events in the Hæmolytic Crisis of Hereditary Spherocytosis", *Blood*, 3: 1381.

DEDICHEN, H. G. (1937), "Epidemic Occurrence of Anæmic Crises in Hæmolytic Jaundice", *Norsk. Mag. F. Laegevinensk*, 98: 279. (Quoted by Crosby, *loco citato.*)

EMERSON, C. P., *et alii* (1947), "The Mechanism of Blood Destruction in Congenital Hæmolytic Jaundice", *J. Clin. Investigation*, 26: 1180.

HORNE, J. L., *et alii* (1945), "Familial Crisis in Congenital Hæmolytic Disease", *Lancet*, 2: 33.

LOUTIT, J. L., and MOLLISON, P. L. (1946), "Hæmolytic Icterus (Acholuric Jaundice) Congenital and Acquired", *J. Path. & Bact.*, 58: 711.

OWREN, P. A. (1948), "Congenital Hæmolytic Jaundice. The Pathogenesis of 'Hæmolytic Crisis'", *Blood*, 3: 1381.

SCHRUMPF, A. (1950), *"Le rôle de la rate dans la sphérocytose familiale"*, *Sang*, 21: 152.

SINGER, K., and WEISZ, L. (1945), "The Life Cycle of the Erythrocyte after Splenectomy and the Problem of Splenic Hæmolysis and Target Cell Formation", *Am. J. M. Sc.*, 210: 301.

YOUNG, L. E. (1947), "Hæmolytic Disorders", *New York State J. Med.*, 47: 1875.

Reviews.

The 1952 Year Book of Orthopedics and Traumatic Surgery (November, 1951–November, 1952). Edited by Edward L. Compere, M.D., F.A.C.S.; 1953. Chicago: The Year Book Publishers, Incorporated. 8″ × 5¼″, pp. 388, with 226 illustrations. Price: $6.00.

THIS Year Book opens with a brief introduction by the editor, Edward L. Compere, in which he mentions the highlights of the previous year. It is an interesting commentary on developments in orthopædics that this introduction is mainly taken up with new drugs for the treatment of arthritis and skeletal tuberculosis. The other main subject mentioned is the choice of prostheses in joint surgery. Reference is also made to interest in the development of better methods in the treatment of fractures and of bone tumours. The abstracts included in the volume are selected from a world-wide range of journals and are presented with a minimum of editorial comment. A short opening chapter on poliomyelitis refers mainly to rehabilitation measures. A chapter on congenital deformities follows. A number of interesting papers on the anatomy, embryology, pathology and physiology of the skeletal system have been grouped together. The epiphyses have brief separate treatment. The chapter on osteomyelitis and other infections is largely taken up with the chemotherapy of tuberculosis. Considerable space is given to tumours, cysts and fibrodysplasia, to arthritis and rheumatism, and to fractures. Most of the rest of the material is grouped according to anatomical regions with concluding chapters on surgical technique, on amputations and prostheses, and on instru-

ments, appliances and bone banks. The volume is freely illustrated and well produced. It should appeal to a much wider field of practitioners than those primarily interested in orthopædics.

Modern Treatment Year Book, 1953: A Year Book of Diagnosis and Treatment for the General Practitioner. Edited by Cecil Wakeley, Bt., K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S.; 1953. London: Published for The Medical Press by Baillière, Tindall and Cox, Limited. 9″ × 6″, pp. 372, with 88 illustrations. Price: 21s.

THIS annual volume has been appearing now for eighteen years, apparently with general acceptance. In the preface to the current volume Sir Cecil Wakeley refers particularly to letters of appreciation sent by practitioners stationed far from hospitals, and he has had this in mind in selecting material for recent volumes. The book is made up of 38 unrelated articles, each by a practitioner of standing in the field concerned. Subjects include vaginal hysterectomy, the use and abuse of penicillin, the chemotherapy of pulmonary tuberculosis and the treatment of trigeminal neuralgia, rheumatic fever, venereal disease, peptic ulcer, hydrocele, chronic backache, hypospadias, *glioma retinæ* (by radium), the menopause, virus pneumonia, mental disorders in pregnancy and childbirth, the arthritic hip, gunshot wounds of the abdomen, carcinoma of various regions and many more. Most of the authors deal with both principles and details of treatment and refer briefly to ætiology, pathology and diagnosis when these are relevant to intelligent therapy.

New Concepts of Hypnosis: As an Adjunct to Psychotherapy and Medicine. By Bernard C. Gindes, M.D., with an introduction by Robert M. Lindner, M.D.; 1953. London: George Allen and Unwin, Limited. 8½″ × 5½″, pp. 288. Price: 15s.

IN this book the author discusses the history, physiological and psychological bases, techniques and application of the so-called science of hypnotism. To put the reader in a suitably receptive state of mind he describes how an adult "blue-baby" underwent a successful appendicectomy under hypnosis when a general anæsthetic was considered too risky. Dr. Gindes also claims to have brought back the memory of an incident in the first birthday of a twenty-four years old patient—the details were confirmed by the patient's mother. He informs us that the Nazis placed elaborate recording devices in nurseries for the purpose of indoctrination "with startling results which can be seen at the present time". His advice that the method should be selected for the individual case is sound; but his comparison of successful hypnotization with the kind of salesmanship which achieves quick results introduces an unpleasant flavour. The critical reader will have some difficulty in determining what is new in Dr. Gindes's methods—the author is not the first to attempt mental analysis under hypnosis; nor is it clear what he means by hypnosynthesis. The application of his methods to fears, improving vision, obesity, faulty concentration, obstetrics and alcoholism (provided that the patient is cooperative) receives special attention. To those who wish to employ hypnotism in treatment this book offers as good information as most others on the subject.

Notes on Books, Current Journals and New Appliances.

Family Doctor. Published monthly by the proprietors, the British Medical Association, Tavistock Square, London, E.C.1. Sole agents for Australia and New Zealand, Gordon and Gotch (Australia), Limited. Subscription for twelve months: 20s. (sterling), including postage.

THE July issue of *Family Doctor*, like previous issues, has something in it to appeal to everyone. J. A. Hadfield sets out to answer the question "Is Punishment the Answer?", and shows how sometimes it is and sometimes it is not. "Along the Seashore", by J. Gordon Cook, puts us on friendly and understanding terms with crabs and squids and other sea creatures, and tells us something of the wealth that is in the sea. The third of Roger Pilkington's articles on "How Your Life Began" is entitled "Beginning to Build a Baby", and describes shortly the early stages of intrauterine life; the diagrams are informative and diverting. An interesting article on comics by R. T. Lewis shows that they are by no means such menaces to children as might be thought. Other subjects discussed are "Facts about Sunshine", holidays, how the oto-rhino-laryngologist has helped in determining the sex of chickens, the Holger Nielsen method of artificial respiration, ringworm of the scalp, "Profile of a Medical Officer of Health", contact lenses, "I Had a Spinal", the true value of alcohol, and cosmetic sense. Pat Sullivan once again provides recipes to make the mouth water, and in an article on "Your Summer Diet" Alan Porter puts protein and carbohydrate in their right perspective. As usual, *Family Doctor* is well produced and attractive; in it the "philosophic pill" may be said to be quite satisfactorily "gilded".

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Immunity, Hypersensitivity, Serology", by Sidney Raffel, Sc.D., M.D.; 1953. New York: Appleton-Century-Crofts, Incorporated. 9½″ × 6½″, pp. 542, with 45 text figures. Price: $8.00.

The author's intention is "to describe the phenomena of immunity in basic terms, especially with regard to resistance to bacteria, viruses and toxins".

"Roentgen, Radium and Radioisotope Therapy", by A. J. Delario, M.D.; 1953. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½″ × 6″, pp. 372, with 65 illustrations. Price: £4 0s. 9d.

The author has "especially stressed . . . the biological reaction to radiation, the diseases that are benefited by this form of treatment, how they are treated and with what dosages".

"Atlas of Medical Mycology", by Emma Sadler Moss, B.S., B.M., M.D., and Albert Louis McQuown, B.S., B.M., M.D.; 1953. Baltimore: Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10″ × 7″, pp. 254, with 248 illustrations. Price: 86s.

The aim is "to present a concise basic plan for clinicians and clinical pathologists who are frequently presented with diagnostic problems dealing with fungous disease".

"Clinical Obstetrics", by Members of the Staff of the Pennsylvania Hospital, edited by Clifford B. Lull, M.D., and Robert A. Kimbrough, M.D.; 1953. Philadelphia: J. B. Lippincott Company. Sydney: Angus and Robertson, Limited. 10½″ × 7½″, pp. 756, with 392 illustrations and eight plates in colour. Price: £5 7s. 6d.

The book describes the obstetrical methods used at the Pennsylvania Hospital; there are 20 authors.

"The Conception of Disease: Its History, its Versions and its Nature", by Walther Riese, M.D.; 1953. New York: Philosophical Library. 9″ × 5½″, pp. 126. Price: $3.75.

The author has traced the various concepts of disease back to their historical sources.

"The Classification of Pulmonary Tuberculosis", by Milosh Sekulich, M.D.; 1953. London: William Heinemann (Medical Books), Limited. 8½″ × 6″, pp. 360, with 148 illustrations. Price: 63s.

The author uses a method of classification of pulmonary tuberculosis "which lays special emphasis on the pathogenesis of the disease, and, at the same time, takes account of radiological and clinical findings and of prognostic and therapeutic considerations".

"An Arterial Systole: A Proposition", by Charles B. Rossiter, M.D. (Dur.), F.R.C.S. (Ed.), L.R.C.P. (Ed.), L.R.F.P.S.; 1953. Auckland: Published by the author. 8½″ × 5½″, pp. 18, with three text figures. Price: 5s.

The author postulates the existence of an arterial systole in the scheme of circulation.

"The 1952 Year Book of Dermatology and Syphilology (December, 1951-November, 1952)", edited by Marion B. Sulzberger, M.D., and Rudolf L. Baer, M.D.; 1953. Chicago: The Year Book Publishers. 8″ × 5½″, pp. 444, with 67 illustrations. Price: $6.00.

One of the Practical Medicine Series of Year Books.

The Medical Journal of Australia

SATURDAY, JULY 18, 1953.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

FRANÇOIS RABELAIS.

FOUR HUNDRED YEARS have passed since the death of François Rabelais, by common consent one of the greatest writers of his time, and held by many *cognoscenti* to be one of the greatest that the world has produced. The great men of the days of Rabelais, as we saw in the case of Leonardo da Vinci, the five hundredth anniversary of whose birth was celebrated last year, were many sided and excelled in several fields of learning. Rabelais, known chiefly today as the author who described the heroic and fantastic adventures of Gargantua and Pantagruel, has been described as the king of jesters. But he was a philosopher also, "thoroughly penetrated with the instincts, the hopes, and the ideas of the Renaissance in the form which it took in France, in England and in Germany". He became a monk and took Holy Orders, being made a canon of the Saint Benedict Abbey at Maillezais. Further—and this is the chief reason for the present discussion—he became a doctor of medicine, and we are told by Jean Plattard that "*sa réputation médicale était considérable*" and that he became "*un des plus fameux médecins du royaume*". Such a man is worthy of our remembrance in this four hundredth anniversary year of his death. The exact date of his death is not certain; the "Encyclopædia Britannica" makes this quite clear; *The Times*, in a leading article of April 9, 1953, accepts the tradition, "unsupported by any documentary evidence", that April 9, 1553, was the date. Gustave Cohen, *professeur honoraire en Sorbonne*, accepts April 9 as the date.

There is a good deal of uncertainty about the year in which Rabelais was born; various dates have been given ranging from 1483 to 1495. Although it is recorded in the Historical Library of the church of Saint Paul, Paris, that Rabelais died on April 9, 1553, at the age of seventy years, this is not accepted. Cohen quotes Abel Lefranc, "the leading authority of the *Études Rabelaisiennes*", as having shown that the date should be brought down to 1494 at least, and Plattard thinks that 1494 should be accepted as the date. Cohen thinks that there is no need to be superstitious or pedantic about the precise date of Rabelais's birth or about the length of his life. "The essential thing is the fact that his books . . . constitute a complete epoch, a whole way of conceiving life and its blossoming, a way of getting it to yield the utmost that it holds." Rabelais's father is said by various authors to have been an apothecary, a tavern-keeper or a lawyer, and it is supposed that he sent his son to a convent at Seuilly and then to a convent school at La Barmette near Angers. Be that as it may, it is certain that the son entered the Franciscan monastery of Fontenay le Comte some time before April 5, 1519, by which date he held a position sufficiently senior for him to sign deeds for the community. After some trouble in which efforts were made by the authorities to check the studies of the Franciscans, a friend of Rabelais, Geoffrey d'Estissac, procured from Pope Clement VII permission for Rabelais to change his order and his abode. He then joined the more scholarly Benedictine order and moved to Maillezais where Geoffrey d'Estissac was bishop. His studies must have covered an enormous field, for they are said to have included medicine, mathematics, theology, astronomy, botany, jurisprudence, the natural sciences and "the romances of chivalry". He was as familiar with Greek, Latin, Hebrew and Arabic as with his mother tongue and he acquired a knowledge of Spanish, Italian, German, English and the Basque languages. But the Benedictine order did not satisfy him and he shed its garb to become a secular priest. Then on September 17, 1530, he entered the faculty of medicine at the University of Montpellier, gaining his baccalaurate in an incredibly short period on November 1. He must have studied to some purpose before he formally entered the faculty; anyhow it is recorded that early in 1531 he gave public lectures on the "Aphorisms" of Hippocrates and on Galen's "Art of Medicine". He gained his doctorate in medicine in 1537. It appears that Rabelais's avocations were for a time at least mixed or carried on concurrently; this was not unusual in those days. The story of his books *Gargantua* and *Pantagruel* is in itself interesting, and should be told at this stage. As we know his work today, *Pantagruel* is in the latter half of his famous book, but it was really written first. It was written "with a definite view to" an earlier work which may have been edited by Rabelais, but which is attributed by no one to his authorship. The earlier work came about in the following way. In 1526 Charles de Bordigné published a mediocre work entitled "*La légende de Pierre Faifeu*", in which the name of Gargantua appeared. (Gargantua and Pantagruel were the popular names of giants in the Middle Ages.) In 1532 (or earlier) there appeared at Lyons "*Les grandes et inestimables chroniques du grand et énorme géant Gargantua*". This is the book which it is thought may have been edited by Rabelais; apparently it contains no trace of the action or other characters of the *Gargantua* that was to be created by Rabelais. The earliest known and dated edition of *Pantagruel* is 1533, and it is thought likely that when Rabelais saw how popular *Pantagruel* proved to be, he wrote his *Gargantua*, deeming that the "*Grandes chroniques*" were not a worthy predecessor to his *Pantagruel*. He described Gargantua as *père de*

Pantagruel and the earliest known and dated edition of his *Gargantua* is 1535.

Medicine in the life of Rabelais has been the subject of special investigation by Donald Slaughter, of Dallas, Texas. He quotes a passage from Etienne Dolet in 1538 about public dissection of the human body "by the most learned of doctors" and argues that this refers to Rabelais. Some authorities have held that it refers to Vesalius, but Slaughter points out that if the quotation refers to Vesalius the demonstration took place when Vesalius was only eighteen years of age. He supports the view of Le Double that Rabelais was the first to make public dissections on the cadaver. Be that as it may, Slaughter states that it is quite clear that Rabelais was one of the pioneers of dissection. He also records that according to the archives at Montpellier, the governing agents were so impressed with Rabelais's work that they allowed the school of medicine two criminals a year to dissect as compared with the six dissected in the preceding hundred years. Rabelais practised at Montpellier, but left there because the King appointed him Master of Requests and he was one of the royal suite at the three-day conference between Francis I and the Emperor Charles V held at Aiguesmorts in July, 1538. We need not try to follow Rabelais in his changes from one place to another. Slaughter mentions some of the well-known men of the day whom he treated and he quotes passages from his books to show what some of his ideas on physiology and other subjects were. He quotes words on the interpretation of dreams "which might appear today in a dissertation on the subject". Martin Dupont writes that Rabelais had been struck with the advantages of hygiene which he thought should be treated with the respect that is due to every positive science. Among the paid positions which Rabelais held was that of city physician of Metz. Slaughter writes that Rabelais saw in medicine a sort of apostolic morality—he sought to combat maladies by "gay literature rich in burlesqueness and clownings". He also thought that even "the poor men afflicted with gout and pox will find solace in reading a few lines of my merrie tales". Slaughter sums this up by saying that Rabelais felt the importance of laughter as a curative agent for the human race. Possibly it was this which influenced Laurence Sterne when he made Tristram Shandy say in 1759 that he wrote his "Life and Opinions" " . . . against the spleen! in order, by a more frequent and a more convulsive elevation and depression of the diaphragm, and the succussations of the intercostal and abdominal muscles in laughter, to drive the *gall* and other *bitter juices* from the gall-bladder, liver, and sweetbread of his majesty's subjects, with all the inimicitious passions which belong to them, down into their duodenums". As a matter of fact it has been stated that if Rabelais had not written his tales of Gargantua and Pantagruel we should have no such books as "Tristram Shandy" and "Gulliver's Travels". Rabelais was prepared to make human physiology suit the purposes of his "merrie tales". His account of the birth of Gargantua is too fantastic not to be mentioned in this account. When Gargamelle, the mother, came into labour the midwives came and began "groping her below", but what they thought was the child was her fundament which had slipped out because of her eating too many tripes. Thereupon an "old ugly trot in the company, who had the repute of an expert she-physician", made her a horrible and restrictive binding medicine which obstructed and contracted her digestive tract. "By this inconvenience the cotyledons of her matrix were presently loosened, through which the child sprung up and leaped, and so, entering into the hollow vein, did climb by the diaphragm even above her shoulders, where the vein divides itself into two, and from thence taking his way towards the left side, issued forth at her left ear."

Rabelais wrote about giants; his writings show that he is to be classed among the giants of literature. His place in medicine is not inconsiderable. He was, as we have seen, one of the most famous medical men of the kingdom, but his work in anatomical dissection gives him a permanent place in medical history. We should do well to remember that in his youth and maturity Rabelais was contemporaneous with Da Vinci, Michelangelo, Raphael, Titian, Dürer, Erasmus, Copernicus, Machiavelli, Cervantes and Vesalius. In recording this fact Slaughter remarks that anyone born and living in this period was played upon by immensely powerful and exciting currents of thought. Time may have provided the opportunity, but the man had to be there to take advantage of it. Anyone coming fresh to the work of Rabelais will be struck at once by its enormous vitality. Life and action are in almost every word that he writes. The censorious will revolt at the crudities which bubble up in his tales. But we must judge the works by the standards of the times in which they were written. Some passages of Rabelais are not what one would choose for reading aloud among the family circle by the fireside, but we need not go so far as to hold, as Irma Dreyfus does in her "Lectures on French Literature", that there are "many passages in Rabelais which no woman could or should read". The "Encyclopædia Britannica" states that:

> The work of Rabelais is the mirror of the 16th century in France, reflecting at once its comeliness and its uncomeliness, its high aspirations, its voluptuous tastes, its political and religious dissensions, its keen criticism, its eager appetite and hasty digestion of learning, its gleam of poetry and its ferocity of manners.

N. Martin-Dupont writes as follows (free translation):

> Rabelais's language is so rich and his vocabulary is so vast, that one man's lifetime would not be enough for him to grasp them; a prerequisite would be an exhaustive study of classical antiquity and of the Middle Ages, as well as of the national idioms which are so diverse and rich in original expressions.

The Times states that in his books are to be found "an amazing erudition, a tempestuous form of satire, which enjoys itself too much ever to become bitter, and such sustained high spirits, such enjoyment of life as will be met with nowhere else in literature". Some students of Rabelais have tried to read into his work occult meanings and deep philosophical teaching. It may be that this can be legitimately done in places, but by and large it surely cannot be possible. *The Times* states that to one who comes to him with an open mind, even the passages of sheer nonsense which have puzzled scholars will suggest a man playing the fool rather than one dealing in obscurities in order to hide a profound message. Cohen quotes an example. When Gargantua was born by way of his mother's external auditory meatus, he at once shouted about with "a mighty, sturdy and big voice" which could be heard in two countries at once: "Some drink, some drink, some drink, as inviting all the world

to drink with him." This has been interpreted as a symbol of the unquenchable thirst for knowledge of the school boy! One can imagine what a time the Freudians could have with Rabelais; the mess that they would make of him would be incredible. It is true that Rabelais does make Gargantua write to Pantagruel that he would see of him "an Abysse and bottomless pit of knowledge"; and he does write that knowledge without conscience is but the ruine of the soul. But philosophy or no philosophy, Rabelais should be read for his excitement, his exuberance, his nonsense and his immensity. *The Times* writes a significant and useful conclusion: "The whole world was his joke, and he was ready to share the joke with anyone who could see it."[1]

Current Comment.

EFFECTS OF HÆMORRHAGE IN MAN.

To understand properly the effects of hæmorrhage one must consider the physiology of the circulation and hæmodynamics. The greater part of the blood volume—66%—is found in the veins, 15% in the arteries and 19% in the arterioles, capillaries and venules. Three main areas, pulmonary, splanchnic, muscle and skin, each hold approximately 30% of the total volume. Taking these and other factors into account, O. G. Edholm has given a critical survey of the effects of hæmorrhage in man.[2]

When blood is lost, the volume of circulating blood is diminished. Compensation for a diminished blood volume can be achieved in a variety of ways. The volume may be restored either completely or partly by the expulsion of blood from depots or reservoirs. A diminished blood volume implies a fall in cardiac output which will result in a fall in blood pressure, unless the peripheral resistance is raised by vasoconstriction. Heart rate will increase if blood pressure falls. What is the relative importance of each of these factors in man? In cats and dogs the spleen is of importance as a blood reservoir, but it has very little importance in man, and there are, in man, no other true reservoirs. The large venous blood volume probably acts as a form of reservoir from venoconstriction. Hæmodilution is another method for restoring blood volume. The rate of this varies greatly in different animals. In the rabbit 20% volume reduction will be completely restored in two hours. In man restoration of a 20% blood loss is not achieved, on the average, until twenty-four hours have elapsed. Hæmodilution is a slow process in man even after small hæmorrhages; less than half the blood lost will be replaced in twelve hours. There is some doubt as to the extent of cardiac output changes in man after hæmorrhages. Some have found that after a venesection of the order of half a litre there is no change or at most a slight one. With larger venesections the cardiac output diminishes significantly. When the subject is lying down hæmorrhages of one litre may have very slight effect on cardiac rate, that is, in the absence of fainting. Blood pressure changes are in many cases slight with small hæmorrhages, excluding those in patients who faint. In a series of volunteers bled to one litre the mean blood pressure fell by only six millimetres of mercury.

It has been generally considered that vasoconstriction of the muscle and skin vessels is one of the important compensatory mechanisms in hæmorrhage. But the blood flow per unit mass of the muscles and skin is very small at rest, so the resistance to blood flow in these regions is very high, before hæmorrhage, in comparison with the vascular resistance of the splanchnic area. Actually after hæmorrhage there is very little change in the blood flow through skin and muscles; the vessels are already highly constricted. It has been shown on the other hand that, after hæmorrhage, there is a considerable reduction in blood flow through the kidneys and after large hæmorrhages the kidneys may be irreparably damaged by anoxia. The evidence at present available indicates that as a result of moderate hæmorrhage of the order of 20% of the total blood volume, the muscle vessels are not constricted; the skin vessels possibly are, but there is a considerable increase in the resistance of the renal and splanchnic vessels.

Fainting after hæmorrhage introduces complications. The number of subjects who faint as a result of venesection varies as the volume of blood withdrawn increases. In fainting there is a marked peripheral vasodilatation. Fainting is almost always transitory, but skin pallor and slow pulse persist even for hours. Battle casualties with severe wounds may lose up to 65% of their total blood volume and still survive, provided the treatment is adequate. A blood loss of over 30% or a blood volume which has been reduced to 70% or less of normal represents a critical level. Blood pressure is usually reduced below 100 millimetres of mercury and the heart rate is increased over 100 per minute under these conditions.

Treatment consists essentially of transfusion and this must be sufficient to replace the deficiency. Up to 2500 millilitres or six or seven bottles of citrated blood given early may be necessary. Heating the patient is the worst form of treatment. Hot water bottles are dangerous. If the patient is heated the skin vessels and underlying muscle vessels will dilate, reducing peripheral resistance and lowering the blood pressure, and diverting blood from other areas. Such effects may well be disastrous. Morphine may be dangerous, for with peripheral vasoconstriction absorption from subcutaneous injections is slow and several doses may be given to relieve pain, and when the blood pressure recovers and subcutaneous flow increases there may be sudden absorption of excess of morphine. In animals morphine in relatively small doses increases mortality after hæmorrhage.

THE TREATMENT OF VESICAL CARCINOMA.

THE innocency of any epithelial tumour of the bladder, as of the urinary tract in general, is notoriously uncertain. R. A. Willis, in his well-known book on the pathology of tumours, states that although it is customary, and for clinical purposes useful, to distinguish between benign papillomata and carcinomata of the urinary tract epithelium, it is impossible to make any real pathological distinction between them. He goes on: "Here, more than in any other situation, there occur tumours showing every possible gradation and every possible sequence from highly organized non-invasive papilloma to disorderly invasive carcinoma." H. P. Winsbury-White[1] found from an analysis of a consecutive series of his own cases that, of 205 bladder tumours which were thought not to be malignant and were treated by cystoscopic diathermy, 21% ultimately proved to be carcinomatous. Wise then is his statement that the treatment of vesical carcinoma begins with the regular supervision of simple bladder growths. In pursuance of this all patients with vesical papillomata should undergo regular cystoscopic inspection throughout life. Winsbury-White recommends that papillomata without cystoscopic features of carcinoma, ascertained after careful investigation, should be treated by cystoscopic diathermy;

[1] In the compilation of this article the following works have been consulted: "The Encyclopædia Britannica"; "The New International Encyclopædia"; "Lectures in French Literature", by Irma Dreyfus, 1896; "Medicine in the Life of François Rabelais", by Donald Slaughter, *Annals of Medical History*, Volume I, 1939, pages 396 and 436; "Vie de François Rabelais", by Jean Plattard, 1928; "François Rabelais", by N. Martin-Dupont; "François Rabelais", *The Times*, April 9, 1953; "A Rabelais Anniversary", by Gustave Cohen, *The Times Literary Supplement*, April 10, 1953; "Doctor Francis Rabelais", by "H.G.S.", *Clinical Excerpts* (date unavailable).

[2] "Lectures on the Scientific Basis of Medicine", Volume I, 1951-1952, British Post-Graduate Medical Federation.

[1] *Lancet*, April 18, 1953.

the need for regular cystoscopic inspection still, however, remains. The difficulty and frequent impossibility of distinguishing between simple papilloma and non-invasive papillary carcinoma are recognized by Winsbury-White, but he declares it essential that a cystoscopist should be able to recognize the early signs of invasive carcinoma. He describes in his paper the criteria by which he himself is guided and emphasizes the need for training in the recognition of malignant changes. It is not his practice to rely on cystoscopic biopsy; delay is unjustified if infiltrating carcinoma is recognized clinically (as it should be), and a negative report is not conclusive. Even in a difficult case in which delayed inspection has been necessary after fulguration, the uncertainty is generally cleared up at the second cystoscopic examination. When the diagnosis in such circumstances is still doubtful, or positive, Winsbury-White prepares to open the bladder on a subsequent early occasion to apply radium treatment, the biopsy specimen being taken at the same time. He points out, at this stage, that an excellent result may be expected from implanting radium into a non-infiltrating papilloma, and suggests that we may be approaching an era in which some simple form of irradiation will be a regular part of the treatment of simple papilloma. In the treatment of carcinoma the relative merits of total cystectomy and radium are still debated, but Winsbury-White considers that both have had a fair trial and it is now possible to compare the results. He puts forward the recent data on this question and, while sympathetic to those who are fighting a rear-guard action in the losing battle to support cystectomy, concludes that radium has produced the better results. He discusses the use of radon seeds and points out that, despite certain advantages of convenience in this form of treatment, evidence is lacking that it has any more than a palliative action on invasive growths. Passing mention is made of treatment with radioactive wire and fluid, which is still in the experimental stage, and of X-ray therapy, which it has so far not been possible to apply to the bladder because of practical difficulties. Much remains to be done on the management of this rather insidious and deceptive condition. The "benign" papilloma is not reliable, although as Winsbury-White points out, simple growths may keep on reappearing for years and years without developing invasive characters. When they do undergo malignant changes, the results of treatment will be unsatisfactory in a considerable proportion of cases, whatever methods are used. Vigilance therefore remains highly important. According to William Boyd, the wise attitude to adopt with these tumours is that well expressed by Aschner when he says that the verdict should be "guilty until proved innocent".

COMMONWEALTH INDEX OF SCIENTIFIC TRANSLATIONS.

THE British Commonwealth Scientific Liaison Offices in London operate a scheme for a Commonwealth Index of Scientific Translations, this scheme being the outcome of a resolution passed at the British Commonwealth Scientific Official Conference held in London in 1946, followed by a similar recommendation made at the Royal Society Scientific Information Conference in 1948. So far an agency has been appointed in seven of the Commonwealth countries. Each agency collects information regarding translations made by the organizations in its own country which are cooperating in the scheme; the information is listed at appropriate intervals of up to a few months, sent to B.C.S.O (London) to copy on standard cards and then distributed to all agencies. Thus each agency maintains a master index. The agency in this country is The Commonwealth Scientific and Industrial Research Organization, Translation Section, 314 Albert Street, East Melbourne, Victoria. It will check the existence of translations when requests for these are received. The master index is not available for circulation to the public. Its purpose is to serve as a check when a translation of a given article is required for work being undertaken. It would help the operation of the scheme if requests could be restricted to papers needed in the prosecution of research in progress and not in anticipation of future needs. It is not the intention that countries or organizations should request translations merely for library holding purposes. It is on this understanding that scientific organizations which may make translations and which are not already members are invited to participate in the scheme and to get in touch with the agency whose address has been given above. The agency acts in a liaison capacity; it is responsible for collecting information about translations held in its own country, for advising B.C.S.O. (London) of these, for maintaining the central index of translations and for assisting research and other people in its own country to obtain copies of translations requested by them and already prepared elsewhere.

THE NATURE OF CARDIAC AND PULMONARY DYSPNŒA.

DYSPNŒA, the major symptom of disordered breathing, differs very much in nature from one clinical state to another. D. W. Richards[1] has considered these differences in cardiac and pulmonary diseases. Dyspnœa occurs whenever the individual's actual ventilation cannot easily be provided by his breathing capacity and is defined as breathing associated with effort or distress, including here both subjective breathlessness and the objective evidences of laboured breathing. The major factors producing dyspnœa are reduced ventilatory capacity with restricted breathing, increased ventilatory work with laboured breathing and increased respiratory stimulus with increased (hyperpnœic) breathing. "Maximum breathing capacity has been used as an index of pulmonary function or of dyspnœa." This takes into account the speed as well as the volume of ventilation. The author has found a better index in "breathing reserve" which is the maximum breathing capacity *minus* the actual ventilation, or the reserve of ventilation still available at any moment. This difference, expressed as a percentage of the maximum breathing capacity, defines quite well the appearance of dyspnœa when it reaches a value of 65% to 70%. The simplest form of dyspnœa, occurring in pulmonary disease, is seen when there is some restriction of the breathing mechanics as in fibrotic lung. In more serious forms of diffuse pulmonary disease there is usually disturbance in the respiratory drive or stimulus. Some modern textbooks state that patients with chronic cardiac failure typically hyperventilate while patients with chronic pulmonary failure do not. This, according to the author, is far from true. The distribution of inhaled tidal air to perfused alveolar spaces is often markedly unequal in many forms of pulmonary disease. Some air spaces are greatly overventilated, others underventilated. There is ventilation of regions having no blood perfusion. To provide for adequate respiratory gas exchange total ventilation must increase. As distribution of inhaled air deteriorates still further, alveolar air stagnates in some parts where active blood perfusion continues, and aeration of the blood becomes inadequate here, even in the presence of total pulmonary hyperventilation. Arterial anoxia then ensues. The elimination of carbon is not so much, if at all, affected. How is the hyperventilation brought about? Evidently there are many chemical and reflex influences, and, too, the final ventilatory performance is influenced by conscious or subconscious psychic effects.

The question of the functional or psychic aspect of clinical dyspnœa is a most important one, in both pulmonary and cardiac dyspnœa, and difficult of analysis. This refers not to true respiratory neuroses but to patients with some pulmonary disease and much dyspnœa and hyperpnœa.

It would be difficult to construct a type of disease in which there occurred simultaneously more different kinds of pulmonary dysfunction than are found in advanced

[1] *Circulation*, January, 1953.

pulmonary emphysema. The progress of emphysema can be considered as falling into four classes. At first there are increased maximum breathing capacity, some hyperpnœa and exertional dyspnœa, but normal aeration of blood. When ventilation deteriorates further, there is inadequate oxygenation of arterial blood, especially in exercise. Still later there is inadequate carbon dioxide elimination and more advanced anoxia. In the most advanced stages there is failure of the respiratory centre and the patients, while dyspnœic, are sometimes not urgently so in spite of profound anoxia.

The basic defect in heart failure, as compared with pulmonary failure, is inadequate performance of heart and circulation rather than inadequate performance of the lungs. The main factors in the production of dyspnœa in cardiac failure are the inability of the cardiac output to carry sufficient oxygen for the tissues, especially in exercise, and to get rid of carbon dioxide, and the stiffening of the lungs with pulmonary vascular congestion. In cardiac failure muscle exhaustion accompanies dyspnœa as a manifestation of inadequate blood flow. This is seen particularly in exercise. Effort of breathing is increased by pulmonary congestion and this is the major factor in the production of dyspnœa in some cardiac cases. In general, however, the dyspnœa of mild cardiac failure appears to be due chiefly to inadequate cardiac output with resulting chemical stimulation of the respiratory centre from reduced oxygen and increased carbon dioxide, while in advanced congestive failure pulmonary congestion is the important factor. Finally there are still patients with what has been called "iatrogenic" heart disease, individuals with a story of severe exertional dyspnœa who have been found to have entirely normal cardiac and pulmonary function, but because of a cardiac murmur, probably present from very early age, have not been allowed exertion to the point of even normal breathlessness. The diagnosis of neurosis is made rather too often in chronic pulmonary disease and perhaps not often enough in rheumatic heart disease with a valvular murmur but no failure.

MALARIA TERMINOLOGY.

MALARIA with its heavy world-wide incidence has been investigated and discussed by workers of many nations in many places and often quite independently. It is not surprising that a great diversity exists in the terms used to describe the disease and all its associated factors. The Malaria Commission of the League of Nations recognized the need for a standard nomenclature and in 1940 published their "Report on Terminology in Malaria". This report is now out of print, but a revised version has been prepared by a drafting committee appointed by the World Health Organization and issued under the title of "Malaria Terminology" as number 13 in the World Health Organization Monograph Series. The drafting committee consisted of Major-General Sir Gordon Covell, Adviser on Malaria to the British Ministry of Health, Dr. Paul F. Russell, of the Rockefeller Foundation, and Dr. N. H. Swellengrebel, Professor of Parasitology in the University of Amsterdam. The monograph is in two parts: the first is a commentary on terms used by malariologists, excluding those for engineering techniques used in malaria control; the second is a simplified but comprehensive glossary, which acts also as an index to the first part, the reader being frequently referred to a fuller explanation in the text instead of the short definition usual in a glossary. Part I has three chapters. The first chapter deals with the malaria parasites and the infections to which they give rise, the second with malaria in the human community and the third with the vector. The drafting committee has obviously been at great pains to find out and understand the varying terms used for the same thing and the varying meanings attached to a single term. On that basis they have provided a standard nomenclature which should be generally acceptable. As an example of their treatment of one particular type of difficulty, we may quote their comment on "The Name Anopheles":

> Some hesitation is often felt as to whether to write *Anopheles*, "Anopheles", Anopheles, anopheles, or anopheline. A good working rule is to employ *Anopheles* only when giving a definite zoological value to the name, and to use anopheles or anopheline whenever it is merely a question of colloquial designation.

Amongst important aspects of the work are the clarification of the zoological nomenclature of the parasites, the illustration of the tissue stages of plasmodia in a series of figures, the definition of the chief rates and indices used in measuring endemicity, and the provision of a systematic method of age-grouping and a scheme for classifying data in relation to splenomegaly. The greatest value of the standardization made possible by this monograph is probably in the epidemiological field, in the objective assessment of results of malaria-control campaigns and the comparison of these results in various countries.

THE MEDICAL RESEARCH COUNCIL OF NEW ZEALAND.

THE Medical Research Council of New Zealand has issued its first annual report and statement of accounts; it covers the activities of the Council for the year ended March 31, 1952. As the document was received on July 1, 1953, we must presume that there has been a good deal of delay in the printing, which is a pity. Such delays are not unknown in Australia. Dr. John Cairney, the Chairman, who is the Director-General of Health of the Dominion, points out in the introduction that medical research has been carried out for many years in New Zealand, but that it was not until December, 1937, that an attempt was made to put it upon a properly coordinated and organized basis. In that year a Medical Research Council was established, but its status was that of a departmental committee. On March 31, 1951, it was superseded by the present Medical Research Council. The old council organized research in many fields and most of it was carried out in collaboration with the Medical School at Dunedin. The old council found that its lack of legal status was a handicap. It could not assure its employees of permanent employment, nor could it provide superannuation benefits for them. Some of its work was of long duration, and as it was dependent on annual appropriations, it had no financial stability and it could not be sure that its long-term work could be carried to a conclusion. During 1951-1952 the Council received a grant of £10,000, and though it is not specifically stated, the implication is that this will be the amount of the annual grant. We are informed that a further defect of the old council was that "discoveries made by its research workers were not adequately protected". We cannot help wondering what this means. Naturally we ask what kind of protection is needed by research workers and then we ask what protection the new Council can give which the old body could not offer. Perhaps this will be explained in a future report. It is to be noted that the Council has appointed several research committees. At March 31, 1952, it had committees on clinical medicine, dentistry, endocrinology, microbiology, neuropathology and neurophysiology, nutrition, island territories, obstetrics and tuberculosis. Throughout the report there appears at the end of every section a list of papers that have been published. Those listed number fifty-two and include many of the greatest interest; they reflect the high standard of medical endeavour in New Zealand.

The Medical Research Council consists of three ex-officio members and seven others. The ex-officio members are Dr. Cairney, Director-General of Health; Mr. F. Callaghan, Department of Scientific and Industrial Research; and Sir Charles Hercus, Dean of the Faculty of Medicine, Dunedin. The others are Dr. P. P. Lynch, Sir James Elliott, Professor F. H. Smirk, Dr. Douglas Robb, Dr. L. Bastings, Dr. R. S. Aitken and Dr. J. P. Walsh. Future reports will be awaited with the greatest interest.

Abstracts from Medical Literature.

PÆDIATRICS.

ACTH Therapy of the Nephrotic Syndrome in Children.

J. METCOFF, C. P. RANCE, W. M. KELSEY, NOBOYUKI NAKASONE AND C. A. JANEWAY (*Pediatrics*, November, 1952) report on 56 courses of ACTH therapy given to 45 children with the nephrotic syndrome. Daily dosage was 150 to 200 milligrammes per square metre given for at least eight and usually ten days. Complete diuresis was obtained in 68% of courses and 75% of children. Induced diuresis and remission were associated with considerable improvement in renal function. Four patients died as a result of therapy. The principal complications were infection, severe hypertension and hypotonicity of the extracellular fluid. Adequate dosage, normal diet without added salt, and possibly a limited period of reduced renal function appeared to favour diuresis. The authors consider that at the present time ACTH therapy is the treatment of choice for the active phase of the nephrotic syndrome in children.

Treatment of Congenital Adrenal Hyperplasia with Cortisone.

J. F. CRIGLER, S. H. SILVERMAN AND L. WILKINS (*Pediatrics*, October, 1952) report studies on three infants with disturbed electrolyte metabolism. Each infant had a genital abnormality (female pseudohermaphrodism) associated with vomiting and weight loss. The authors' observations lead them to suggest that the hormones produced by the abnormal adrenals cause sodium loss. In treatment sodium chloride is first given, parenterally if necessary, in amounts up to four to seven grammes daily, as found necessary to produce well-being. Then cortisone is added in amounts required to produce maximal depression of the abnormal 17-ketosteroid excretion. In some infants it will still be necessary to add desoxycorticosterone (D.C.A.) to maintain normal electrolyte balance. With D.C.A. the salt intake may be reduced, and implantation of D.C.A. pellets performed after the dose is determined.

Prepubertal Malignant Melanoma.

K. F. TRUAX AND H. G. PAGE (*Ann. Surg.*, February, 1953) describe what is apparently the first reported case of a true prepubertal malignant melanoma in a two and a half years old boy, with death from metastatic disease a year later. The literature contains only four cases in which prepubertal melanomata have been diagnosed histologically and have also been clinically malignant; although in all these four cases metastases occurred, none of the patients have died after radical surgery in the next twelve, seven, three and two years. Two other cases were found in the literature in which the malignant melanoma was transplanted through the placenta, the mother and child dying shortly after delivery. In a further two cases congenital malignant melanoma resulted in the death of the child soon after birth, but the mothers were free from the disease. For the first two and a half years the child reported by these authors had developed normally, and the onset of the malignant melanoma could not be directly traced to influence by maternal hormones. Also, there was no evidence of precocious puberty. The lesion on the scalp had been present since birth, but no change had been noticed in its appearance.

Epilepsy in Children.

D. A. POND (*J. Ment. Sc.*, July, 1952) discusses psychiatric aspects of epilepsy in children on the basis of an investigation of about 150 children at the Maudsley Hospital. Children referred to this hospital nearly always show behaviour disorders; the actual seizures in these cases to a great extent were a secondary problem. The effect of brain injury is discussed. The author states that characteristically it produces aggressive, unstable and unpredictable children. Attention and concentration are poor, although intelligence quotient readings are not abnormal. The children may suffer from *grand mal* and/or psychomotor attacks, but never classical *petit mal*. The electroencephalogram either is normal or shows focal abnormalities. The severest behaviour disorders appear to be associated with temporal rather than frontal electroencephalographic disorders. With psychomotor attacks disturbance of consciousness is incomplete, and a confused dreamy state prevails; psychological disturbances are common. Rejection, over-protection or sibling rivalry can be seen in the epileptic child. The importance of the fit depends mainly upon the attitude of the parents to it. The parents' attitude to the child is often the reason for recommending that the child be sent to an epileptic colony. Referring to treatment, the author states that phenytoin is the first drug for *grand mal*. Amphetamine can be useful and has a quietening effect on children in contrast to the effect on adults; it is particularly useful for the hyperkinetic and irritable child. Phenobarbitone at times is said to cause increased irritability.

Combined Diphtheria and Whooping-Cough Prophylaxis.

G. BOUSFIELD (*Med. Officer*, June 28, 1952) states that the future of diphtheria immunization is intimately bound up with whooping-cough prophylaxis. At present whooping-cough is the dreaded disease and whooping-cough prophylaxis is more popular than diphtheria prophylaxis, but permanent security against diphtheria implies immunization of all children during the first few months of life. A combined diphtheria and whooping-cough prophylactic is desirable. One in use composed of *Hæmophilus pertussis* vaccine and diphtheria alum-precipitated toxoid occasionally caused sharp local reactions, sometimes followed by development of sterile abscesses. In 1949 it was shown that poliomyelitis was likely to be severer after injections of combined prophylactic material than after injections of either diphtheria or whooping-cough prophylactic given separately. As a result the use of this form of combined prophylactic decreased. The number of diphtheria prophylactic injections was decreased by the use of P.T.A.P. At the same time as P.T.A.P. was introduced, the author injected purified formol diphtheria toxoid subcutaneously without producing any noteworthy reactions at all. Three injections produced an optimal Schick conversion in young children. Later the author combined this material with an *H. pertussis* vaccine and obtained a 99·58% Schick conversion rate in 475 children treated and investigated. The reaction rate following injection of this combined prophylactic in 758 children was then compared with the reaction rate following injections of the plain *H. pertussis* vaccine in 521 children. The rate for the first was 4·22% and for the second 4·41%. There was also no significant difference in the Schick conversion and reaction rates following intramuscular and subcutaneous injections. This means that if the combined prophylactic described is used, immunization against diphtheria and whooping-cough can be carried out with only three injections, and the risk of complications following poliomyelitis after the injections is reduced. However, the author suggets that if poliomyelitis becomes prevalent during a course of combined injections, the diphtheria prophylaxis should be completed with subcutaneous injections and the whooping-cough prophylaxis be postponed; and that at times when poliomyelitis is prevalent, diphtheria prophylaxis should proceed without interuption, but whooping-cough prophylaxis should be postponed. The author gives details of the combined prophylactic.

Transient Diabetes in Infancy.

S. L. AREY (*Pediatrics*, February, 1953) defines *diabetes mellitus* as a syndrome characterized by hyperglycæmia and glycosuria with abnormal metabolism of fat and protein. He reports the occurrence of a diabetic state in a premature infant who suddenly lost weight and became dehydrated on the thirteenth day of life. The fasting blood sugar content was 555 milligrammes *per centum*. Administration of insulin produced dramatic improvement and was continued for two months, by which time the result of the glucose tolerance test was normal. Four similar cases found in the literature are briefly described.

Prolonged Obstructive Jaundice.

D. Y. Y. HSIA AND S. S. GELLIS (*Am. J. Dis. Child.*, January, 1953) have studied liver function tests in a series comprising 94 infants with biliary atresia, 23 with inspissation of bile due to erythroblastosis, 30 with inspissation of bile of unknown cause, four with infective hepatitis and five with obstructive jaundice due to miscellaneous causes. The serum alkaline phosphatase determination and the flocculation tests were not of use in differentiating the causes of obstruction. The flocculation tests were helpful in distinguishing between obstructive jaundice and such causes of jaundice as infective hepatitis, syphilis, galactosæmia, congenital cirrhosis and infective mononucleosis. Bile in the stools or urobilinogen in the stools suggested incomplete obstruction. A slowly rising serum bilirubin level suggested biliary atresia, a rapidly falling trend suggested hepatitis or inspissation of bile due to erythroblastosis, and a slowly falling or variable trend suggested inspissation of bile of unknown cause. The authors consider that surgery should be delayed to enable repeated studies to be performed. Surgery is indicated if there is consistently no bile in the urine, duodenal

juice and fæces, if the bilirubin level steadily rises from an initially low level, if the results of flocculation tests are negative, and if there is no blood incompatibility between mother and baby. Further delay of surgery is necessary if these conditions are not fulfilled.

Teaching Infants to Walk.

MAURICE H. HERZMARK (*J. Pediatrics*, April, 1953) states that flat feet most commonly arise from infants learning to walk on a hard flat surface; this encourages them to evert the foot and bring the longitudinal arch into contact with the flat smooth floor. He observed that native children learning to walk on irregular pebble-strewn ground did not evert the foot, but maintained the arches of the foot. He designed a rubber mat closely studded with knobs one-quarter of an inch high and has had a number of infants learn to walk on this. The foot cannot flatten because the knobs make contact with it while arched, the toes grip the irregular surface, the foot muscles are exercised, and normal feet with intact arches develop.

ORTHOPÆDIC SURGERY.

The Acrylic Femoral Head Prosthesis.

ROBERT AND JEAN JUDET (*J. Bone & Joint Surg.*, May, 1952) present an analysis of 400 patients operated upon between one and five years ago with insertion of the acrylic femoral head prosthesis. They use Hueter's short anterior incision to approach the hip joint. In the first 100 cases the capsule was sutured at the end of operation, in another 100 it was freely resected; results were similar. The authors now resect only a small medial area of the capsule over the head of the femur in order to minimize the risk of impairing the blood supply of the head and neck. They state that the correct position for the stem is along the true axis of the neck and that if the head of the prosthesis is seated in a position of either *coxa vara* or *coxa valga*, pain occurs. Resection of part of the head removes most of the pain, and remodelling of the acetabulum is necessary only to obtain a close fit of the prosthesis. The number of cases with and without acetabuloplasty are the same; there is no significant difference between the results. The results are assessed by the use of a numerical evaluation, with "points" for pain, movement and gait. The term "starting rate" is used for the number before operation and "final rate" for the number at the last examination. The "amelioration rate" is the difference between these two. Results are bad when the amelioration rate is between 0 and 3, poor between 3 and 6, good between 6 and 9, excellent above 9. The mortality rate was 1·8% during the first month after operation. Wound infection occurred in 3·8% of cases. The authors describe a method by which during the last year they have successfully treated acute infection in four cases. The method is one of surgery with combined local and general antibiotic therapy. The authors state that persistent pain may be due to operation on patients with senile changes, obesity with circulatory changes in the legs, certain general diseases, and, above all, lack of sufficient determination to cooperate, or to technical faults, such as poor fitting of the head into the socket, too lateral a position of the head in the acetabulum, and faulty position of the stem in the neck. Thrombophlebitis occurred in 7·3% of cases. Results in 217 cases of osteoarthritis were bad in 17%, poor in 19%, good in 47% and excellent in 17%. The authors found that the amelioration rate depended on the age of the patient. The average starting rate of the patient was 6·8 and the final rate 13·1. In other words, before operation the typical patient had acute pain so that he could not work, very limited movement so that he could not put his shoe on, and walking restricted to one or two hundred yards; whereas after operation the pain was slight or intermittent and permitted work, he could put his shoe on, and he could walk a good distance with, or even without, a stick. The authors were surprised to find that the final rate depended on the starting rate only to a moderate degree. This means that more can be done for a patient with a severely disabled hip than for one retaining good function. In very old people, replacement by an acrylic head is sometimes good and safe treatment of recent fracture of the neck of the femur. In the usual age group for fracture of neck of the femur, that is, fifty to seventy years of age, the only indication for the use of an acrylic femoral head is when the fracture is subcapital or when the head is porotic. The authors have operated upon 47 patients with non-union following fracture of the neck of the femur. The average final rate was about 13·5. This treatment has also been used in post-traumatic and in old septic arthritis, with good results. In 108 adult patients operation has been undertaken for congenital dislocation of the hip. With anterior dislocations, the chief benefit for the patients is relief of pain. With posterior dislocations, results were bad in 28% of cases, fair in 36% and good in 36%.

Fractures of the Carpal Navicular.

CARRUTH J. WAGNER (*J. Bone & Joint Surg.*, October, 1952) presents the results of treatment in 37 cases of aseptic necrosis of the proximal fragment of a fractured navicular. Three methods of treatment were used: prolonged immobilization, removal of the avascular fragment and removal of the entire navicular. The author states that the best results were obtained with immobilization until revascularization of the proximal fragment had occurred. The price for somewhat better results was the long period of immobilization and its associated economic inconvenience. The average period of immobilization was eleven months, and in all cases immobilization consisted of a skin-tight plaster cast from the elbow to and including the hand with the wrist in dorsiflexion. The thumb to the distal joint was incorporated in a position of opposition, in such a way that it could be just cleared by the index finger in its flexion arc. Use of the hand was encouraged. Casts were changed on an average of every five weeks. The final results were tabulated after an average follow-up period of three and a half years. In all cases union occurred, and the results could be considered good in all but one case. In this case union was obtained, but partial collapse of the proximal fragment occurred in spite of immobilization. When prolonged immobilization was unacceptable, fairly satisfactory results were obtained with excision of the proximal fragment. Eighteen patients were treated by this operation. All but two of these were operated upon about four weeks after injury, when the first cast change revealed devitalization of the proximal fragment. Half the group are now free of symptoms, and all but two have returned to their former occupation. The author states that X-ray examination of these wrists invariably shows a proximal migration of the capitate with medial shifting of the lunate, apparently in an attempt to obliterate the empty space. This shift occurs shortly after removal of the fragment and soon reaches a maximum. It is perhaps this disturbed relationship which is responsible for symptoms when excessive demands are placed upon the involved wrist. The entire navicular was excised in five cases, two of comminuted fractures of the navicular with associated radial fractures, one of avulsion of the tubercle combined with a high waist fracture, and two of high waist fractures combined with perilunar dislocation. The periods of follow-up averaged three years; the results were poor. The two patients with perilunar dislocation required arthrodesis of the wrist within a year of the injury; one patient, a labourer, now requires a brace while working and shows significant weakness of the thumb in gripping; two patients have moderate restriction of motion and weakness of grip, but lead sedentary lives not requiring heavy use of the hand; and one of them has a radial deviation of the hand which cannot be corrected passively.

Separate Neural Arch.

G. R. ROWE AND M. B. ROCHE (*J. Bone & Joint Surg.*, January, 1953) have tried to determine whether the fundamental lesion of spondylolisthesis is congenital in origin or not by ascertaining the incidence of neural arch separations in the fœtal and neonatal periods, in childhood and in maturity extending into senescence. Dissections carried out on the cadavera of 50 stillborn infants, varying in age from approximately six months of gestation to term, failed to demonstrate a defect suggesting separation of the neural arch. Attempts to produce separation of the neural arch by manipulation of stillborn infants failed; thus birth injury is not believed to be a significant cause. Paucity of the lesion in young children also supports this contention. Examination was also made of 20 specimens of cleared and stained human fœtus, aged from about ten weeks of gestation to term. Neither accessory nor double centres were found in the neural arch. The authors believe that there is therefore no proof that the lesion is congenital. From examination of 4200 skeletons they found that, although the incidence of separate neural arch varied with ethnic group and sex, it remained constant with age between twenty and eighty years. X-ray examination of 140 children revealed an incidence of neural arch defects midway between the frequency in the adult and the total absence at birth. The authors conclude that the lesion of spondylolisthesis is acquired, but how it is acquired is not yet understood.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

LXXI.

GALL-STONE DISEASE.

DISEASES of the gall-bladder are very common in Australia, particularly when compared with England. In England peptic ulcer is the main cause of painful dyspepsia, whereas in Australia it is usually gall-bladder disease. The chief reason for this would appear to be dietary. England has had two wars, during both of which her population was on a deficient fat and diminished meat diet. In Australia there was abundance of both these foods.

In spite of our increase in knowledge of metabolic biochemistry, particularly of the sterol group, we still seem to be a long way from knowing how to prevent the formation of cholesterol stones. The altered cholesterol metabolism in pregnancy and in fat individuals seems to increase the liability to form gall-stones, but does not make it inevitable. The other known cause of gall-stones is infection, and it is probable that once infection has occurred the subsequent development of gall-stones is certain.

The main symptoms of gall-bladder disease are pain, vomiting, dyspepsia and jaundice, but as jaundice is such a localizing sign, I will discuss only the diagnostic value of pain, vomiting and dyspepsia.

First take dyspepsia, or chronic indigestion. A most careful analysis must be made of what the patient really means when he says he has indigestion. Frequently he just means "belching". In most cases this is functional and due to air-swallowing, self-induced to relieve a feeling of discomfort in the epigastrium and therefore of very little use as a differentiating symptom. The other main condition referred to as indigestion is a feeling of fullness or bloating in the epigastrium after meals, and the more intelligent or better informed patient may have noticed that this is worse after fatty meals. In other cases it is borborygmi, the significance of which I cannot explain. Yet again it may be excessive flatus, which is probably due to colonic stasis and a heavy vegetable diet.

Of all these, only the fullness or postprandial bloating is characteristic of gall-bladder disease. It is seen radiologically that the gall-bladder may not empty well in chronic cholecystitis; therefore, as bile is the chief saponifier of fats, there is probably a deficient digestion of the fat. But is this presence of undigested fat in the duodenum the cause of the epigastric fullness? X-ray examinations with barium meals in gall-bladder disease show little stasis in the duodenum or stomach. Is the discomfort due to the slow emptying of the gall-bladder, and does its slow reflex contraction produce the full, over-distended feeling which is somewhat analogous to the discomfort of the over-distended urinary bladder when social etiquette prevents its immediate evacuation? Maybe œdema, from chronic inflammation of the cystic duct, slows the rate of emptying. Practically there is no doubt that diminution of fat in the diet will reduce the discomfort, as also will cholagogues which increase the rate of emptying, and these facts may be used as therapeutic tests.

Vomiting is mainly reflex from severe pain and will therefore occur in any dyspeptic condition if the pain is severe enough; therefore vomiting is of little diagnostic value, except that the most profuse vomiting usually occurs in the condition with the most severe pain, which is usually pancreatic.

Now when we consider pain, it can be divided into two main components: firstly, the mechanical intermittent colicky pain produced by the repeated contractions of a hollow tube trying to rid itself of an irritant; secondly, the inflammatory component, which is a dull aching pain due probably to inflammation and stretching of the peritoneal covering of a viscus.

If we consider first the colicky pain, it will help to remember that the gall-bladder develops as an *Anlage* from the primitive foregut, which is a mid-line developmental structure, and that most of the viscera whose diseases give trouble in the differential diagnosis develop from this tube. At the upper end of the tube is the œsophago-gastric region at the level of a hiatal hernia, then the lesser curve of the stomach and duodenum with their tendency to develop peptic ulcer, followed closely by the liver and gall-bladder diverticulum and the pancreatic bud, with the small bowel filling up the interval to the appendix.

Now colicky pain produced by disease at any of these levels is almost invariably first referred to the mid-line, the level in the mid-line depending to some extent on the level of the pathological condition; for example, œsophageal orifice spasm is felt under the xiphisternum; pylorospasm, gall-bladder spasm and pancreatic colic are felt midway between the xiphisternum and umbilicus; small bowel colic is felt between this point and the umbilicus, and appendiceal colic at the umbilicus. Thus we see that the colicky pain is not going to be of very much use as a differentiating factor unless the patient is very conscious of its site. Most patients just say "a pain in the pit of the stomach", and cannot localize its level very accurately.

Usually the degree of intensity of the pain is not of very much value, as patients vary so much in their threshold to pain and in the vividness of their descriptive powers; but in general the gradation of intensity is pancreatic (easily first), followed by gall-stone colic, and then pylorospasm and œsophageal orifice pain. It may be noted that the intensity approximately conforms with the size of the contracting tube; that is, the small pancreatic duct produces the most intense pain and the wide fundus of the stomach in the diphragmatic hernia the mildest pain.

Now if the contraction of the hollow viscus continues long enough, it will usually be associated with the development of inflammation and œdema of the involved viscus and its peritoneal covering. This is the second component of the pain complex, and it is referred to the anatomical site of the involved viscus. Thus the œsophagitis produced by a diaphragmatic hernia is felt as a burning pain under the sternum and through to the back. When a duodenal ulcer starts to perforate and becomes adherent to an adjacent viscus such as the pancreas, which is retroperitoneal, the pain becomes localized and appears as a continuous boring pain in the back. In gall-bladder disease, as the bladder distends or inflammation occurs the pain moves to the right subcostal margin, over the gall-bladder; and as inflammation spreads to irritate the adjacent part of the diaphragm it may be referred to the tip of the shoulder, or, particularly in those cases in which the gall-bladder is very deep and lies against the posterior peritoneal wall, the pain may be referred through to the back. With pancreatic disease the pain remains in the epigastrium and passes over to the left side as the disease extends along the body of the pancreas and through to the back as the retroperitoneal tissues become inflamed. With appendicitis the pain will, of course, be localized to the right iliac fossa in a typical case. Boas's sign, which is elicited in some cases of gall-bladder disease, consists of an area of hyperæsthesia on the back about the level of the lower angle of the right scapula and is usually elicited only when the gall-bladder is distended.

Thus we see that the early stages of these five diseases are all much the same, and differentiation can be made only as time goes on and inflammation extends to adjacent localizing structures. Hence the many diagnostic errors.

One of the greatest causes of confusion in gall-bladder disease is the frequent coexistence of disease in one or more of the viscera mentioned above, with a consequent mixing-up of symptoms and signs.

Recurrent appendicitis, duodenal ulcer, pancreatitis, diaphragmatic hernia and hydatid disease are all quite common associated conditions, and it is often difficult to decide which disease is producing the symptoms or whether more than one is responsible, and whether all conditions should be dealt with at the same time. The fact that gall-stones are often silent should make it a *sine qua non* that a thorough exploration is always made at operation, particularly palpation of the diaphragmatic orifice, as even expert radiography may not succeed in demonstrating a hiatus hernia. The mere demonstration of gall-stones by radiography, particularly if the gall-bladder is functioning well, does not mean they are the cause of the syndrome of pain, vomiting and dyspepsia.

Other common conditions to be excluded are renal tract abnormality and coronary disease. The former is usually fairly easily excluded on the distribution of the pain and by radiography. The latter is more difficult to distinguish, but from a practical point of view the acute attack should always be treated as a coronary attack if doubt exists, as delay in operation on an acutely inflamed gall-bladder can cause no harm, but operation on a patient with coronary occlusion may possibly lead to a death under anæsthesia.

Regarding treatment, the first important thing to realize is that once infection has occurred it will keep on flaring

up, as is the case in all glandular structures, in spite of prophylactic treatment, and that a chronically infected gall-bladder will almost certainly develop gall-stones if the patient lives long enough.

The second thing to remember is that once a gall-stone is present it is usually only a matter of time before symptoms and complications will develop. Of course, we know that many post-mortem examinations are made which reveal gall-stones and there is no mention of any symptoms suggesting them in the history, but in many cases no questioning has been directed towards the expected symptoms.

From these remarks it is evident that if gall-stones are found, even if accidentally in routine investigation or during a laparotomy for some other condition, then the patient should be advised to have a cholecystectomy. The reason for this is that the removal of an uncomplicated gall-bladder by a competent surgeon is devoid of risk, but the operation on a complicated gall-bladder carries a definite mortality; and we are constantly having to perform these complicated operations now in elderly people who have known that they had gall-stones for years and have postponed operation until it has become an absolute necessity, and then their general myocardial and pulmonary state causes grave worry and in some cases death.

Now what are these complications? The first is acute inflammation, which in itself will rarely cause death, as with proper treatment it will mostly subside. The second is the passage of a gall-stone into the common duct, which will always require operation; the longer this is delayed the higher will be the mortality, as cholangitis and liver failure develop. The third is the development of carcinoma; although the exact relationship to gall-stones is not proven, it is almost unknown to find carcinoma in a gall-bladder without stones, and once it has developed cure is almost hopeless. The fourth is the ulceration of a gall-stone into the intestine with the development of small bowel obstruction from the gall-stone with its high mortality.

Regarding the perennial question of the treatment of the acutely inflamed gall-bladder: a vogue for immediate operation occurs about every ten years or so, and a recent flood of literature in America and subsequently in Australia has again brought it into prominence. The crux of the position is which form of treatment will produce the less mortality and morbidity—to operate or to wait. It is remarkable that this plea for early operation is always raised by young surgeons, and never by the older and more experienced ones. The young surgeon does most of the emergency surgery, and in many cases of "acute abdomen" the diagnosis is in doubt and he operates. He finds an acutely inflamed gall-bladder; and being young, and not desiring to lose prestige by having people say he could not do it, he removes it with a struggle and gets away with it. Of course, in 95% of cases he will get away with it, but in the other 5% he will strike gross trouble and leave permanent damage or cause death. Now death or damage from keeping the patient with acute gall-bladder disease under observation is very rare. By this I mean not that every acute inflammation of the gall-bladder will eventually subside, although in my experience it will in 90% of cases, but that the additional delay which has saved 90% of these operations does not damage the outlook in the 10% in which the condition does not subside, because a simple conservative drainage operation will be all that is necessary; at a still later date, if it is necessary, and it usually is, a second operation of cholecystectomy can be performed without risk.

Now what are these dangers of immediate operation?

Firstly, hæmorrhage from the cystic artery is very prone to occur, because the œdema makes the artery difficult to find and when found it is very friable. A clamp put on it may easily cut right through or pull off; and then there is profuse hæmorrhage, and wild clamping may be indulged in to find the spurting vessel, which leads to crushing of the common bile duct with subsequent slough or stenosis of this vital structure.

Secondly, the gall-bladder itself is friable and may rupture; and since it is filled with virulent organisms, occasionally anaerobic, this may give rise to general peritonitis because protective omental adhesions have been broken down by the surgeon, or gross infection of the abdominal wall may occur.

Thirdly, the common bile duct is grossly swollen and œdematous, so that it is difficult to palpate and expose. Fortunately, of course, it is not often necessary to open the common bile duct in acute gall-bladder surgery, but opening it must carry increased risk of damage to this essential tube. The lumen is œdematous; therefore great difficulties are encountered in passing a probe, and a stone is both tricky and dangerous to remove.

What, on the other hand, are the risks of watching and waiting? It is usually stated that perforation into the general peritoneal cavity with the development of bile peritonitis may occur. This risk is slight, as the longer the patient waits, the greater is the amount of omentum which adheres around the gall-bladder until it becomes completely walled off; thus the worst that occurs is a small localized abscess between the abdominal wall, the gall-bladder and the omentum. This can be safely drained at any time without risk of general peritonitis. Perforation of the gall-bladder into the general peritoneal cavity is likely to occur only if a previous operation has bound the omentum down to the pelvis, so that it cannot collect around and wall off the gall-bladder.

The other complication is stated to be the lowering of the general condition of the patient from toxæmia and septic absorption and the development of pneumonia. This risk in the modern days of antibiotic drugs is negligible. Therefore the safest treatment is to watch and wait.

The patient should be in hospital under competent nursing supervision, and the following regime is commenced. A four-hourly record of pulse rate and temperature is commenced, and the gall-bladder mass, if one is present, is outlined on the skin; if a mass is not present, the degree of tenderness and rigidity is noted. Heat is applied to the tender area, antibiotics are given (I usually use penicillin), and a fluid diet only is allowed. In twenty-four hours the patient's condition is reassessed. If the pulse rate is over 120 per minute and there has been a steady rise, and if the local tenderness or mass is still greater, then it is probable that the condition is not going to subside and preparation is made for laparotomy. But remember that it is against all surgical principles to proceed with a difficult operation in the face of acute spreading inflammation; therefore in most cases it is wiser and safer to perform cholecystostomy and drainage. However, this is not a rigid rule, and the procedure will depend on what the local condition looks like and on the experience of the operator. I think that in most of these acute cases, if cholecystectomy is performed, it is most easily and safely done by finding a plane of cleavage in the œdematous layer between the muscular and subserous layers of the gall-bladder, the surgeon starting at the fundus and working towards the cystic duct. If, on the other hand, after twenty-four hours the pulse rate has not risen much and the mass has not enlarged (and this is the usual finding), then it is safest and wisest to keep on watching. If this policy succeeds and everything settles down, then let the patient return home and come back again in two months for reinvestigation and probable cholecystectomy. In some cases, however, the condition seems to remain as chronic hydrops; the acute inflammation settles, but the gall-bladder remains distended and tender, and in these cases operation should be performed about ten days after cessation of acute inflammation.

In routine cholecystectomy when should the common bile duct be explored? This operation is performed much more often nowadays, approximately 30% of patients requiring the procedure. I consider that a history of jaundice, a dilated common bile duct, a large cystic duct with the presence of small stones in the gall-bladder, a thickened pancreas, a single facetted stone in the gall-bladder or much mud in the gall-bladder requires in every case exploration of the common bile duct and the passage of a probe into the duodenum; if any pathological process is found, the common duct should be drained by a "T" tube. This procedure adds a little time to the operation, but it may save a subsequent exploration; and if no pathological condition is found, it does not increase the risk of operation and at worst may mean a day or two longer in hospital.

G. R. A. SYME
Melbourne.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Melbourne, on March 11, 1953.

Diaphragmatic Hernia.

DR. RUSSELL HOWARD spoke on the subject of diaphragmatic hernia, and as an introduction demonstrated the anatomy of

the diaphragm and the sites of hernial orifices. He said that according to those sites, herniæ could be classified. On the basis of such a classification, the distribution of a recent series of 12 cases at the Children's Hospital was demonstrated. The distribution was as follows: Herniation through the foramen of Morgagni (retrosternal), no case. Herniation through the foramen of Bochdalek (pleuro-peritoneal hiatus), two cases. Herniation through the dome of the diaphragm, no case. Lateral diaphragmatic hernia, two cases. "Hiatus hernia"—para-œsophageal, no case; congenital defective crura, four cases; congenital short œsophagus, three cases; traction hernia, one case; sliding hernia, no case.

Dr. Howard said that as herniation could occur through sites of widely different distribution in the diaphragm, it was reasonable to suppose that different organs could be involved. That, in fact, was true, and furthermore different syndromes could be identified according to the site of herniation and the organs involved.

In the neonatal period a diaphragmatic hernia could present as an acute surgical emergency with cyanosis, dyspnœa and absent breath sounds over part of the chest. In the series of 12 cases, three were of that type. Herniation could occur through the pleuro-peritoneal hiatus or the dome of the diaphragm or be of the "lateral diaphragmatic" type. The herniated elements consisted of small and large bowel and perhaps spleen or liver. Radiological examination would show bowel shadows in one pleural cavity with mediastinal displacement to the opposite side. The infant might die in a matter of minutes or hours, and it was therefore imperative to perform an immediate or early operation, according to the degree of distress.

A second syndrome was caused by a type of hernia which was due to defective development of both crura. The hernia passed upwards into the mediastinum, and its contents consisted of part or all of the stomach. The syndrome was characterized by vomiting, the vomitus sometimes containing altered blood, and failure to thrive during the first year of life. Occasionally pressure on the heart by the displaced and dilated stomach produced severe syncopal attacks. In one case the parents heard a swishing noise in the chest. Physical signs in the chest might be absent; but a skiagram might show the thickened coverings of the stomach projecting into the pleural cavity, and a barium bolus and meal examination would confirm those findings. It was important to realize that, in this type of hernia, the stomach was not always in the chest, and therefore physical signs and radiological appearances might be deceptive. For the same reason symptoms might be intermittent. The treatment was operative, with repair of the diaphragm by suture in front of and behind the œsophagus. Four such cases appeared in the present series.

A third syndrome was that of the congenitally short œsophagus with resultant hiatus hernia. There was much argument as to the frequency of this type, but in the series there were two undoubted cases and a third almost equally certain. In this syndrome, the infant presented because of gastro-œsophageal reflux, with vomiting, which sometimes was projectile and often with blood-stained vomitus. Congenital hypertrophic pyloric stenosis was frequently suspected. The infants were slow and difficult feeders from birth, failed to thrive and were not infrequently anæmic. Œsophagitis was common, and sometimes the sequel of œsophageal stricture occurred. The clinical features of stricture were first noticed when solid food was added to the diet.

Œsophagoscopy demonstrated the characteristic peptic œsophagitis and a stricture if that was present. A barium bolus and meal examination would show a gastro-œsophageal reflux and the herniated stomach. When the œsophagus had been fully mobilized and the stomach had been returned to the abdomen, operative repair of the hernia would greatly relieve the symptoms, but might not completely eliminate the gastro-œsophageal reflux. Duodenal ulceration might also be present in such cases.

The type of hernia described as the "traction" hernia occurred in infants who initially had gastro-œsophageal reflux in the absence of hernia. As a result of œsophagitis and contraction in length of the œsophagus, the stomach was drawn into the thorax; thus a secondary hiatus hernia was caused. Clinically the patient in such a case would present with the features of œsophageal stricture. The series contained one such case.

A fourth syndrome was characterized by the sudden onset of symptoms in a previously healthy child, because of an increase in intrahernial pressure. It might produce either vomiting or actual strangulation and could occur in any of the types of hernia described. Early or immediate operation was indicated. One such case occurred in the series.

Dr. Howard then discussed the operative approach to the conditions he had described. He said that in the case of congenitally short œsophagus approach must be made through the thorax in order to mobilize the œsophagus adequately. If it was thought desirable, the incision along the eighth rib could be continued onto the abdominal wall and the peritoneum opened; that enabled the stomach to be drawn down whilst repair of the defect was accomplished. For a hernia due to defective crura Dr. Howard said that he preferred an abdominal approach, the patient being tilted with the head up, gravity being thus allowed to assist in the exposure of the diaphragm. Foramen of Morgagni herniæ were approached in a similar manner.

Other types were best exposed by the abdominal part of an abdomino-thoracic incision, which could be continued into the thorax if necessary.

The Syndrome of Cardio-Œsophageal Relaxation.

Clinical Features.

DR. HOWARD WILLIAMS said that there was a syndrome in infants and young children which was characterized clinically by repeated vomiting and hæmatemesis, radiologically by reflux of barium through an open cardio-œsophageal sphincter into a dilated œsophagus, and in some patients by œsophagitis. Various writers had attributed the syndrome to different pathological lesions. However, congenital short œsophagus, diaphragmatic hiatal hernia, relaxation of the cardio-œsophageal sphincter and œsophagitis could all produce the syndrome.

During the past three and a half years 24 patients with the syndrome had been studied clinically, and it seemed most probable that symptoms in the majority of those patients were due to an inefficient sphincteric mechanism at the lower end of the œsophagus. Often there was difficulty in establishing an exact ætiology in the individual patient, especially if œsophagitis was present or if a diaphragmatic hernia was suspected by the radiologist. Observation over a period was necessary before a final opinion could be given, and even then doubt could exist. However, sufficient evidence was available to describe accurately the clinical features and part of the natural history of the disorder, to indicate methods of management and to show how radiology and endoscopy could help to establish a diagnosis.

Symptomatology.

Vomiting.—Vomiting was the outstanding and constant feature. There were no distinguishing features about the vomiting; often the vomitus welled up into the mouth and overflowed onto the pillow, but frequently the vomiting was projectile in nature and closely simulated that seen in pyloric stenosis. It commonly occurred immediately after a feeding, but could occur at any time, while in some cases it was worse when the infant was laid down. Vomiting commenced usually in the first week of life, often as soon as the infant was fed, but occasionally before, and in a few cases not until the infant was some weeks or months of age. It usually occurred daily at first, in some cases after almost every feeding, while in others it was variable. It was only later, usually after some months or even a year, that there were remissions from vomiting of several days', weeks' or months' duration. In the majority of cases the duration of the remissions from vomiting increased during the second year, and vomiting ceased during the end of the second or the third or fourth year.

Hæmatemesis.—In some form hæmatemesis occurred at some stage of the illness in almost all patients. It was usually noted during or soon after the commencement of vomiting, but could be the initial symptom of the illness and develop a few hours after birth before the infant was fed. At times it was delayed until the infant was some months of age or even older than one year. The blood was usually altered in colour, as a result of contact with the acid gastric secretion, and was noted as dark brown, chocolate or coffee coloured streaks or specks which were intimately mixed with mucus. The material was commonly not recognized as blood, either by the mother or by the nursing staff if they were inexperienced. Occasionally bright blood was vomited, but the amount was usually small.

Melæna.—Although bleeding from the lower end of the œsophagus was usually manifested as hæmatemesis, sometimes a melæna stool was passed. The results of occult blood tests on the stools were frequently positive.

Constitutional Symptoms.—According to the frequency and severity of the vomiting so the infants either lost weight or

gained weight only slowly. In the few with severe vomiting, dehydration occurred and intravenous therapy was necessary. As the infant became older and the severity of the vomiting lessened and remissions occurred, growth became more normal. Some infants were very difficult to manage, as they were of the hyperkinetic type. In that group frequent vomiting caused further irritability and helped create a vicious cycle of vomiting and irritability. Other infants were placid and did not seem to be emotionally disturbed by vomiting. Only in two cases of the severe type with frequent vomiting and repeated hæmatemesis did anæmia and stunting of growth occur.

The Diagnosis.

Dr. Williams said that the clinical pattern of vomiting from a very early age with hæmatemesis of the nature just described was most suggestive of an abnormality at the lower end of the œsophagus. Frequently the diagnosis was not suspected clinically because the presence of blood in the vomitus was not recognized; either the parents did not realize that coffee grounds or chocolate-coloured streaks or specks were altered blood, and did not mention those features to the clinician, or he in turn did not question the mother or nurse to find out if they did occur. Another reason for misdiagnosis was failure to appreciate that projectile vomiting was common in such a disorder. That misconception probably arose from the belief that vomiting was always due to regurgitation of gastric contents through a lax cardio-œsophageal sphincter.

In two cases severe vomiting in the neonatal period with some dehydration had suggested an upper bowel obstruction, while repeated projectile vomiting in several others had led to a diagnosis of pyloric stenosis. Vomiting in a hyperkinetic child suggested a diagnosis of "pylorospasm"; and if the mother was nervous and uncertain in handling the infant, feeding mismanagement was diagnosed. A careful clinical history and observation usually gave sufficient evidence to suspect an œsophageal lesion.

Tests for occult blood in an infant with repeated vomiting were worth while, for if the results were positive, they suggested the possibility of an œsophageal lesion. One such baby was referred to the radiologist and the diagnosis confirmed.

Radiological Diagnosis.—Three very important signs were the keys to the diagnosis: the first was the demonstration of inefficiency of the cardio-œsophageal sphincteric mechanism; the second was the presence of gastric reflux; the third was the presence of dilatation and atonia of the œsophagus. In some cases there was difficulty in deciding whether a hernia through the diaphragmatic hiatus existed.

The Course of the Disease.

The course of the disorder was very variable; in some cases vomiting ceased after a number of weeks or months, but in the majority after one to two years or a little longer. In two cases the symptoms had persisted. Those patients whose symptoms subsided after some months developed normally and had no abnormal physical signs. However, in the larger number of cases even when the patients were symptom free, radiological examination showed that gastric contents still regurgitated into the œsophagus from intermittent relaxation of the sphincteric mechanism.

Management.

The natural history of spontaneous loss of symptoms in the majority indicated that the management was medical. Reassurance of the parents was most important, for it was very distressing for a mother to see her baby repeatedly vomiting. Gentle handling, careful feeding in the semi-propped position and small feedings at three-hourly intervals, often with a "Bengerized" milk, were the main features of the feeding regime. If the infant was of the hyperkinetic type, then sedation with phenobarbital, a quarter of a grain three times a day, often helped. No other treatment than those simple measures seemed necessary. The atropine group of drugs was given to a few patients, but no apparent benefit followed.

Finally Dr. Williams issued a warning and said that there were a number of surgeons who believed that the larger number of patients with the symptoms and radiological signs described had a sliding hernia through a lax diphragmatic hiatus and advised early surgical treatment. The clinical experience of the patients at the Children's Hospital indicated that almost all lost their symptoms and were well. Certainly a number still had constant œsophageal reflux and a lax hiatus. Whether that was a disadvantage could not be answered. There did not seem to be sufficient evidence to warrant any operative procedure in that group. The risk of surgery appeared to be greater than the risk of complications developing in the patient when treated medically.

Radiological Features.

DR. FRIEDA PLARRE said that the radiological findings in cases of cardio-œsophageal reflux in infancy had been described in 1947 by Neuhauser, who encountered 12 cases in three years. In February, 1950, the first case was met with at the Children's Hospital. The patient was a male infant, four and a half months of age, with similar radiological features—namely, constant patency of the diaphragmatic hiatus, dilatation and atonia of the whole length of the œsophagus and constant reflux of gastric contents, with stasis in the œsophagus when the patient was recumbent. The child had vomited since birth, but differed from those in Neuhauser's series in that he had vomited blood. On that account, œsophagoscopy had been performed and revealed reddened, swollen mucosa resembling gastric mucosa in the distal two to three inches of the œsophagus. Examination of the patient when eighteen months old revealed considerable clinical improvement, while radiological examination showed that gastric reflux was still present. The œsophagus at that time was of normal calibre in the upper two-thirds; the lower third was more dilated than usual and easily filled by gastric reflux, and coarse longitudinal folds in the mucosal pattern suggested an intrathoracic stomach. Œsophagoscopy, under general anæsthesia, at that stage, however, revealed normal œsophageal mucosa macroscopically, and the œsophagus was apparently normal in length, with a patulous cardio-œsophageal orifice.

Dr. Plarre then showed skiagrams to demonstrate the appearance of the normal œsophagus in infants and young children, with peristalsis and dilatation of the cardio-œsophageal orifice during the passage of a bolus of thick barium cream. In contrast, the calibre of the œsophagus was regular, with a "pencil-point" cardio-œsophageal opening when distended by continuous drinking of thin fluid barium from a feeding bottle. The narrowed "pencil-point" opening was maintained if the babies were fed in a steep Trendelenburg position. After completion of the feeding, complete competence of the cardio-œsophageal sphincter was demonstrated by pressure on the stomach with radiological examination in the supine and inverted postures. Momentary reflux of barium from the stomach could occur in normal babies if they were badly fed. It was important, therefore, that all babies should be fed with a suitable teat, so as to avoid excessive air-swallowing or rapid hungry gulping. A small feeding of not more than two to three ounces for a small baby or four to six ounces for a baby six months of age was found to be most satisfactory. The babies were held upright to bring up wind, and often momentary reflux of barium would then occur. However, once the baby had eructated and was comfortable again, the pylorus would empty normally. At that stage, no gastric reflux could be induced in normal babies by posturing or by pressure on the stomach. The examination excluded pyloric and duodenal obstruction, both of which could cause œsophageal regurgitation. Another cause of mild intermittent gastric reflux was observed. In two weak babies, who had failed to thrive, mild intermittent gastric reflux was presumed to be due to poor tone of the hiatal mechanism, as well as to general atonia.

Over the last three and a half years, 24 cases had been met with in which the clinical features were similar to those of the first case—namely, vomiting of obscure nature, usually dating from birth, in many cases with altered blood in the vomitus, and occasionally with frank hæmatemesis. The youngest patients were eleven days and three weeks old respectively. All showed continuous or intermittent gastric reflux, with varying degrees of dilatation and atonia of the whole length or of the distal third of the œsophagus. The majority of the patients had improved clinically and lost all symptoms after a period varying between a few weeks and several months, but only a small number showed a completely normal œsophagus, with competent hiatal mechanism on follow-up examination. The variety of radiological appearances seen with repeat examinations caused some difficulty in differential diagnosis.

One patient was investigated as possibly suffering from an œsophageal ulcer, as she had vomited and had several hæmatemeses during the first month of life. Gastric reflux was demonstrated radiologically, with constant narrowing of the œsophagus at the level of the ninth thoracic vertebra, but œsophagoscopy revealed a patulous cardio-œsophageal orifice without any ulcer being visible. Later radiological examination showed persistent gastric reflux, with dilatation of the lower portion of the œsophagus, although clinically the patient had been symptom-free for more than two years after solid foods were introduced to the diet.

Five of the patients showed at either the initial or the follow-up examinations the appearance of intrathoracic stomach, with mucosal folds running obliquely or transversely in the small ballooned segment above the diaphragm. In some patients of that group, a small intrathoracic protrusion of the stomach could be missed, as it was difficult to persuade some toddlers to take sufficient barium into the stomach to fill the fundus—the intake was so slow that it did not keep pace with pyloric emptying. In one of those cases, the intrathoracic protrusion of stomach was clearly seen to slip in and out of the diphragmatic hiatus; but when the child was examined two weeks later, only the incompetent cardio-œsophageal sphincter could be seen, without any herniation. All the patients progressed well clinically, and although the radiological follow-up was still incomplete, the longest being three years, there was some evidence from the group that the condition of patients with gastric reflux and a small intrathoracic stomach could improve spontaneously, both radiologically and clinically.

Only one of the 24 patients failed to show much relief of his symptoms. After two years, he still vomited if given solids and was very difficult to feed at all. Radiologically, he showed constant gastric reflux with atonia of the œsophagus and constant narrowing at the level of the eighth thoracic vertebra, so that an early stricture was suspected. Œsophagoscopy, however, showed a dilated œsophagus, a patulous cardio-œsophageal opening and œsophagitis, but no evidence of stricture.

Four of the six patients exhibited narrowing of the lumen of the œsophagus at the level of the seventh and eighth thoracic vertebræ. That narrowing, with a dilated distal lumen, suggested the possibility of an intrathoracic stomach. However, the mucosal folds in the dilated lower third were never oblique or transverse, but always longitudinal and occasionally a little coarser than normal. In addition, endoscopy revealed no narrowing of the lumen at the level seen radiologically, and the mucosa in the lower third macroscopically was œsophageal and not gastric.

In conclusion, Dr. Plarre said that she considered that the early radiological diagnosis of stricture of the lower end of the œsophagus in the presence of reflux could be very misleading, owing to the occurrence of spasm, and the radiological diagnosis of any permanent anatomical deformity, such as intrathoracic stomach, should also be made cautiously. Repeated skiagrams should be prepared after suitable intervals, and should be correlated with clinical and endoscopic findings.

Discussion.

DR. R. V. HENNESSY spoke briefly on the endoscopic appearance of the œsophagus in the condition of cardio-œsophageal relaxation. He said that in typical cases, the outstanding feature was the flabbiness and flaccidity of the œsophageal wall. The œsophagus at the distal end resembled the appearance in cardiospasm or achalasia in adults. However, whereas in cases of cardiospasm there was difficulty in finding the cardiac opening, in cases of cardio-œsophageal relaxation the œsophagoscope passed easily into the stomach as if there was no cardiac sphincter. As the child became older, the coordination of the detrusor and sphincter muscles improved, and at the same time there was a spontaneous remission of symptoms.

DR. ROBERT SOUTHBY said that infants suffering from congenital hypertrophic pyloric stenosis sometimes developed hæmatemesis. That was not diagnostic of cardio-œsophageal reflux.

He asked the question whether, in view of the fact that many of the infants were hyperkinetic, there was any evidence of pylorospasm, as shown by a delay in emptying of the stomach. He also asked if there was any information on gastric acidity.

Dr. Williams, in reply to Dr. Southby, said that he had followed the clinical courses of one hundred and four infants suffering from congenital hypertrophic pyloric stenosis, and only one infant had vomited blood. The stomach emptying time was reasonably rapid, and there was no evidence of an abnormal hold up of stomach contents. Histamine had been administered to eight of the infants, and the total acidity of gastric contents was high.

DR. KATE CAMPBELL said that she had been interested in the condition of cardio-œsophageal relaxation for some time, and was of the opinion that it occurred more in private than in public hospital practice. A high percentage of the infants concerned had a history of vomiting coffee grounds. Dr. Campbell said that she believed that there was a combined effect of pylorospasm and a relaxed cardiac orifice. Most infants suffering from the condition either were themselves nervous or had nervous mothers. The radiologists often remarked that the œsophagus could be dilated with air to an amazing degree. With reference to hiatus hernia, Dr. Campbell mentioned that the passage of a stomach tube sometimes resulted in a reduction. Posture of the infant was important in assisting reduction of the hernia.

DR. HENRY SINN remarked that one infant whom he had treated appeared to have a disordered swallowing reflex. The condition of cardio-œsophageal reflux was a problem for the physician, and it was the prerogative of the physician to consult a surgeon when necessary. Dr. Sinn asked whether there was a relation to possetting in normal infants.

Dr. Williams, in reply, said that possetters, when examined, did not exhibit persistent or intermittent reflux.

DR. D. DOWNING asked if there was any sex incidence.

Dr. Williams replied that the distribution between the sexes was equal.

DR. JOHN PERRY asked whether an endoscopic biopsy of the lower end of the œsophagus was of any use in the diagnosis of œsophagitis. Could the mucosa of the lower end of the œsophagus resemble gastric mucosa?

Dr. Williams, in reply, said that biopsies should be carried out where possible, but the interpretation was difficult. Brown Kelly had investigated, by means of endoscopic biopsies of the lower end of the œsophagus, a series of apparently normal babies selected at random. A surprising number of the examinations revealed gastric mucous membrane one or two centimetres above the cardiac orifice.

DR. B. W. NEAL quoted the case of an infant who had presented with the clinical features of an intussusception. Death occurred suddenly, and necropsy revealed a huge diaphragmatic hernia.

Dr. Howard said that death was probably due to a syncopal attack, caused by increased intrathoracic pressure.

DR. JOHN O'SULLIVAN asked the means of differentiating congenital from acquired cases of short œsophagus.

Dr. Howard, in reply, said that often operation provided the sole answer. Each case in the series which he had quoted had similar features. There was no œsophagitis, and the œsophagus was definitely short, ending two inches above the diaphragm. Both patients were young infants. If radiological examination in two planes at right angles showed the œsophagus passing straight down into the stomach with no sign of stricture, and if endoscopic examination revealed no œsophagitis, a congenitally short œsophagus probably existed.

DR. JOHN COLEBATCH said that although it was reasonable to attribute hæmatemesis to cardio-œsophageal reflux, vomiting and failure to thrive might be due to an entirely different factor, such as pylorospasm. As Dr. Williams had mentioned that reflux could be present for several years without vomiting, it seemed reasonable to suggest that. An autonomic imbalance involving more than the cardiac opening might be the underlying disorder, and the possibility of a nervous background should be investigated. It was important to reassure the mothers of those infants. Dr. Colebatch asked Dr. Williams whether, apart from hæmatemesis, any of the clinical features were due to reflux.

Dr. Williams, in reply, said that the syndrome had many facets, many of which were incompletely understood. In many cases reflux merely acted by facilitating, not causing, the vomiting.

DR. COLIN MACDONALD said that reflux frequently occurred in normal infants, from causes such as rapid feeding and inexperienced feeding, or if the infant was upset and "jumpy". For that reason one must be very wary of attributing reflux to pathological causes. There was a danger of popularizing a rare condition, and a radiological examination should be carried out with the infant in the supine and inverted positions, after it was quiet and settled.

DR. S. W. WILLIAMS asked if a symptom-free diaphragmatic hernia should be subjected to surgical operation.

Dr. Howard, in reply, said that most diaphragmatic herniæ produced symptoms, and a radiological examination was not made unless symptoms existed. When discovered during infancy, all diaphragmatic herniæ, with the exception of the congenitally short œsophagus, should be subjected to surgery. Strangulation or pressure effects, which could be fatal, were serious possibilities.

DR. V. L. COLLINS stressed the danger of attributing a variety of symptoms to a lax cardiac orifice. Vomiting in the infants concerned might be due to generalized neuro-

muscular incoordination of the whole alimentary tract. A lax cardiac orifice and possibly pylorospasm might be contributory causes only. Local abnormalities in the œsophagus, such as œsophagitis and œsophageal ulceration, might cause certain symptoms and contribute to vomiting.

Dr. Plarre agreed that conservatism in radiological diagnosis, as advocated by Dr. Macdonald, was necessary. There were probably gradations between reflux in the normal infant and reflux resulting from a permanently relaxed cardiac orifice.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

UNDESIRABLE IMMIGRANTS.[1]

[From "The Voice of Truth in Defence of Nature", by Mingay Syder, M.D., Geelong, 1861.]

IT should be borne in mind that the great object we had, as a body, in migrating here was to better our several worldly conditions. We have, most of us, been squeezed out of our native land, by the force of circumstances of some kind or other, and numbers have been drawn here of late by the irresistible attraction of the world's idol—the mammon of our gold fields.

The "elegant" victim of Baden and Aix-la-chapelle, in my humble opinion, had better remain where he is—this colony was not selected by its discoverers and first settlers as a nursery for the idle, dissipated, hypochondriac, phthysical, dyspeptic, hypochondriac, neuralgic, worn out constitutions or for the "prostitutes" and other fungi of Europe, and, until it has become what it was calculated for—a flourishing and highly civilized nation—and can truthfully boast of all the social, domestic, intellectual, moral, and other comforts and blessings Europeans would (if they had the means) enjoy at home, invalids of any kind had better not chance a change in this country.

Special Correspondence.

LONDON LETTER.

(By OUR SPECIAL REPRESENTATIVE.)

Child Health.

PROFESSOR ALAN MONCRIEFF, Nuffield Professor of Child Health at London University, in his Newsholme Lecture at the London School of Hygiene and Tropical Medicine drew attention to the fact that, while infants were regarded by the State as a priority group, and the health of the schoolchild was supervised by the School Medical Service, the pre-school child, the "toddler" age, received little attention unless obviously ill. He argued that, as the State had now assumed responsibility for the public health and sought to encourage the prevention of disease, it should provide a comprehensive service and do much better than at present for the pre-school child. The School Medical Service already had the responsibility for handicapped children over the age of two years, and there was a case for the inclusion of all children of pre-school age under the same service.

A dilemma which often faced the State in matters of health was whether compulsion was desirable if education failed. Education was preferable to compulsion, which in Great Britain automatically produced an "anti"-group. He mentioned the success of the diphtheria immunization campaign in which modern educational methods were used, and he felt that the State had been premature in abolishing compulsory vaccination before educating the public on the risks of smallpox, particularly in these days of rapid air travel.

[1] From the original in the Mitchell Library, Sydney.

Professor Moncrieff believed that the provision of State nurseries for poorer people was justified as a part of preventive medicine. It introduced the child to community living and provided companionship. If day nurseries were regarded as part of the preventive health service, then they should be free.

In the last forty years the School Medical Service had achieved remarkable results, but there was a need for a reorientation in the scope of the work. He suggested that the school doctor should be concerned in the life of the individual school, taking an active or advisory role in the programme for physical education, the teaching of sex education, in problems of school hygiene, lighting and ventilation of classrooms, the design of desks and seats, as well as the prevention of infectious diseases.

The State, having entered the field of social welfare, had not made sufficient provision for the education of the people in prevention. It had produced demands for rights without the recognition or acceptance of compensatory obligations. There was a general attitude of taking something out of the national pool and putting nothing back. The State promised the best medical facilities available and there was a rising demand not for the minimum basic provision but for the optimum. The stage might soon be reached when the parents would demand as a right to have everything done for them and refuse to do anything for themselves.

Skin Reactions from Antibiotics.

The Ministry of Health has issued a note on skin reactions in doctors and nurses administering antibiotics. It has been prepared by a small expert committee and its distribution to medical, nursing, dental and pharmaceutical journals has been advised by the Standing Medical Advisory Committee and the Central Health Services Council.

Recently the attention of the Ministry of Health was drawn to the fact that some district nurses had suffered from dermatitis after having given injections of streptomycin and penicillin to patients. Investigation showed that, while not common, the trouble did occur throughout the nursing profession both in and out of hospital and the following advice has therefore been issued.

It is realized that the technique here recommended following expert advice and *ad hoc* experiments, whilst in conformity with the practice of many doctors, differs considerably from that usually taught to nurses. Urticaria of the face and hands is known to occur in a proportion of those who administer antibiotics by injection. It results from sensitization produced by contact of the solution with the skin, and is believed to be caused much more often by streptomycin than by penicillin. Contamination by the solution of the skin of both hands and face can readily occur when the syringe is held vertically at eye level and air expelled from it before injection: bubbles bursting at the tip of the needle then liberate a fine spray of the solution. In order to prevent sensitization, this operation must not be conducted in this way. The air should be expelled from the syringe with the needle still in the bottle from which the solution has been withdrawn. Care should be taken to support the piston during and after withdrawal, so that further air does not enter. Special care must be taken to ensure that the needle is firmly attached to the syringe so that no sudden leakage occurs under pressure. Contamination of the hands with solution can still take place if the needle used for withdrawal is removed and another substituted for the injection. This is commonly done, either because a wide-bore needle facilitates withdrawal of viscous fluids, or because it is believed that perforation of the rubber cap blunts the needle. This belief is unfounded: it has been shown by experiment that piercing these rubber caps as many as 100 times does not affect the sharpness of the needle. The second precaution advised is therefore that the same needle be used for both withdrawal and injection. This is particularly necessary when giving streptomycin, and since this solution is not viscous, as fine a needle may be used as is desired. After use the syringe should be rinsed out in plenty of water, and the doctor or nurse should then immediately wash the hands to rid them of any traces of solution left on them.

It must be remembered that these antibiotics are not the only possible causes of this type of skin affection.

Making the Most of Nursing Manpower.

Reviewing the field of nursing when he addressed the Association of Matrons at King's College Hospital, London, the Minister of Health, Mr. Ian MacLeod, said that indications were that the nursing profession, which had seen many changes in the thirty odd years since its existence

was first recognized by Parliament, might be facing an era of changes more far reaching than any it had yet contemplated. The report of the Nuffield Provincial Hospitals Trust on the "job analysis" of the work of nurses in hospital wards had been described as a "mine of information". The Minister said that his Standing Nursing Advisory Committee had, at his request, begun a study of the report, and he had been informed that they had in mind a series of practical experiments in ward organization to test some of the conclusions to which the report seemed to point. He was confident that, should the experiments point to the desirability of fundamental changes in organization, nurses would all be ready to accept loyally changes about which they might personally feel considerable doubt. There was one object only—to provide, with the limited human resources available, the best possible nursing service for patients.

Discussing mental nursing, the Minister said that the memorandum which he had issued recently to mental hospital authorities recommending certain measures to deal with their acute staffing difficulties, was an attempt to tackle, on realistic lines, a hitherto intractable problem. It was not his object still further to dilute the professional nursing staff; on the contrary, it was hoped to provide a secure foundation on which to build in time an adequate staff of trained mental nurses of the right calibre. The experience of the general hospitals had already shown that the bold resort to the employment of subordinate nursing staff produced dividends in the shape of record levels of both trained nurses and student nurses. He looked to the mental hospitals to benefit from this experience and to demonstrate the soundness of the process to their own great advantage. In regard to manpower it was essential in the hospital service that the best use should be made of all available staff. In the nursing field this was particularly important, since while the increase in the supply of nurses had changed the problem from one of general shortage to one of distribution, present trends suggested that they might be unable to maintain the same rate of increase as up to the present time. For the first time since 1948 the number of student nurses undergoing training had dropped slightly from 51,648 in June, 1952, to 51,621 in September, and then to 50,475 in December. This must mean that the peak had been passed. The succeeding age groups on which they drew were not getting larger as the years went on. The fact that hospital authorities had to seek higher approval for any increase in their existing total of nurses should lead to a better distribution to the benefit of the undermanned hospitals like those for tuberculosis and mental illness.

Of particular interest was the new training syllabus recently issued by the General Nursing Council, with its more practical approach, its opportunities for a wider basic training and, above all, its emphasis on the preventive aspect of nursing. In the long run the Health Service should be judged rather by the amount of sickness it prevented than by the amount it succeeded in curing, and the nurse had her part to play in the preventive processes.

Discussing the National Hospital Service Reserve, the Minister said that there had been a welcome increase of 8000 recruits to the Reserve during the previous year—making a total of 32,000 towards the peacetime target of 100,000—fewer than 500 of these new enrolments were those of trained nurses. This made the total number of trained nurse members 2400. He appealed for close cooperation in the building up of the Reserve not only of trained nurses but of nursing auxiliaries, upon which hospitals would largely depend for the staffing of static first-aid posts and mobile first-aid units in the event of war.

Whatever changes might be indicated by the various discussions and experiments which were proceeding, it was only through the influence of the matrons that they could be made fully effective and of benefit to patients and staff alike.

Correspondence.

THE JOHN ADEY FUND.

SIR: In September next Dr. John Kellerman Adey is to retire from the Victorian Mental Hygiene Department. To honour him on this occasion, and to mark our appreciation of his long service in the teaching of psychiatry to both graduates and undergraduates, it has been decided to take steps to establish a John Adey Fund in the University of Melbourne to further the teaching of psychiatry.

The actual use to which the fund is to be put must depend on the amount contributed, and must be left finally to the discretion of the Faculty of Medicine; but it is our hope at least to provide for an annual prize, preferably for examination in psychiatry at the undergraduate level. Until the Faculty finds it desirable and appropriate to include such an examination in the course, we would hope a prize could be awarded for an essay on a psychiatric subject, and available to undergraduates and recent graduates.

This is not the place to review John Adey's many services to psychiatry, to students and to his colleagues, or to recite the long list of his hospital, academic, professional and military activities. All who have been associated with him, and members of both the public and the medical profession generally, are invited to join with us in honouring John Adey on this occasion by subscribing to the fund.

Contributions, which are allowable income tax deductions, should be made out to "University of Melbourne Adey Fund" and forwarded to the Registrar, University of Melbourne, Carlton, N.3, Victoria.

Yours, etc.,

J. V. ASHBURNER,
President, Mental Hygiene Medical Officers' Association, Victoria.

Mental Hospital,
Kew,
Victoria.
July 5, 1953.

Obituary.

HILDA JOSEPHINE GARDNER.

WE are indebted to Dr. John Perry for the following appreciation of the late Dr. Hilda Josephine Gardner.

Dr. Hilda Gardner, who died in Melbourne on May 18, 1953, began her medical career in South Australia, the State of her birth, where she graduated from the University of Adelaide in the year 1912. In each year of her medical course, including the final year, she gained first place, the last success securing for her the position of senior resident medical officer at the Adelaide Hospital. Her thoroughness manifested itself early in her life, when after a successful and distinguished medical course she ensured her post-graduate training by serving terms at the Adelaide Children's Hospital and later the Women's Hospital, Melbourne. During the first World War she married Dr. John Forrest Gardner, a South Australian, who practised at Richmond, Victoria. Dr. Hilda Gardner's facility for a sympathetic understanding of domestic as well as academic problems no doubt sprang from her devotion both as a wife and as a mother.

Whilst her formative years were spent in South Australia, where the influence of her family and her primary education was felt, her years of contribution, from which has accrued a vast wealth of influence, were spent in Melbourne. In the year 1929 she was appointed to the Royal Melbourne Hospital as assistant bacteriologist, and from this time her life was devoted to laboratory work. Devotion inadequately describes her coveted capacity to immerse herself completely in the requirements of her bench work. Such a quality has produced scientists of the top rank, but these have no doubt been devoid of the added tasks of guiding a busy routine laboratory whilst maintaining active consultative contact with the medical staff. Long evenings spent after hours were usually the result of many daily interruptions when she graciously gave her time to those coming to discuss a clinical problem. She maintained active contact with clinical medicine both in the wards and in her own department, where she personally prepared and tested allergens, desensitizing patients when necessary. In 1934 she undertook the additional burden of serology, simultaneously taking full control of the bacteriology department. Her excellent techniques and her meticulous care won her a high reputation as a serologist, and later when she became responsible for the hæmatology laboratory, it was perhaps this branch in which she obtained her highest reputation. During the second World War, her department was selected by the late Dr. Charles Kellaway, then Army Director of Pathology, as a training laboratory for service pathologists. This task, in addition to her routine duties aggravated by wartime drain on technical staff, was accepted with eagerness by Dr. Gardner and discharged with the same thoroughness that she gave to the training of her assistants in prewar years.

Her lectures in clinical pathology, designed for students in her own hospital, found their way far beyond this limited sphere, but those students of her own hospital were more fortunate in that she conducted an excellent course of practical pathology in a well-designed and equipped laboratory next door to her own. In this laboratory she instructed trainee technicians on behalf of the Society of Laboratory Technicians of Australasia, for whom she was an ardent worker and a member of the examining body. Dr. Gardner was actively concerned with the interests of clinical pathology in her own State and over a wider Commonwealth domain. Her active membership of the Australasian Association of Clinical Pathologists from its inception testifies to this. In 1951, she was honoured by The Royal Australasian College of Physicians by being made a Fellow of that body, in recognition of her contributions to her field of practice.

Of Dr. Hilda Gardner as a student, resident medical officer, wife, mother and head of a department a little has been said, a little and yet enough to establish in our memory the vision of an unusually capable, devoted and accomplished woman. Her solidarity had come to be taken for granted in that way which reflects the love for her of those who worked in her sphere. Dr. Gardner's life has enriched the fame of her already distinguished family, and those who were privileged to work near her will be anxious to extend their sympathy to her brother, Sir Howard Florey, and her daughter, Dr. Joan Gardner, of Melbourne.

Post-Graduate Work.

NORTH-EASTERN MEDICAL ASSOCIATION.

Post-Graduate Week-End.

THE annual post-graduate week-end course conducted by the North-Eastern Medical Association (New South Wales Branch of the British Medical Association) will be held at the Base Hospital, Lismore, on August 1 and 2, 1953. Subjects to be discussed are as follows: "Acute Head Injuries" and "Surgical Approach to Intractable Pain" (Dr. J. Dowling); "Chest Injuries" and "Emergency Thoracic Surgery" (Dr. H. Windsor); "Value of Sigmoidoscopy in General Practice" and "Investigation and Treatment of Diarrhœa" (Dr. Bruce Hall). Intending members should communicate with the secretary, Dr. N. J. Rogers, 24 Conway Street, Lismore, as soon as is convenient.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

PROGRAMME FOR AUGUST.

Overseas Lecturer.

DR. FRANK GERBODE, general and thoracic surgeon, of San Francisco, will lecture on Friday, August 21, 1953, at 8.15 p.m., at the Royal Australasian College of Surgeons, Spring Street, Melbourne, on "The Present Status of Surgery of the Œsophagus". The fee for this lecture will be 15s., payable in advance to the Melbourne Permanent Post-Graduate Committee. Resident medical officers may attend at half rates. Those who have already paid an annual subscription to the Committee are invited to attend this course without further charge.

Country Lecture.

On August 21, at 8 p.m., Dr. R. F. A. Strang will lecture at Ballarat on "The Use of Cortisone and ACTH". The fee for this lecture is 15s., and enrolments should be made with the Secretary of the British Medical Association (Victorian Branch) Subdivision, Dr. J. P. J. Griffiths, 6 Dowling Street, Ballarat. Those who have already paid an annual subscription to the Committee are invited to attend this course without further charge.

Courses for Part II of Diplomas and F.R.A.C.S.

The following courses will continue: bacteriology for D.O., D.L.O. and D.G.O.; radiodiagnosis and pathology for D.D.R.; psychiatry for D.P.M.; and pathology for F.R.A.C.S.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 13, 1953.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	5(3)	..	..	..	..	..	..	5
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	6	..	..	..	1	..	7
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	4(3)	8(6)	..	..	..	..	..	12
Diphtheria	9(7)	1(1)	7(4)	..	4(3)	1(1)	..	..	22
Dysentery (Bacillary)	..	2(2)	..	6(6)	..	..	..	..	8
Encephalitis	..	..	..	2	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	..	8(3)	..	..	3(2)	..	1	..	12
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	2	..	..	..	..	..	2
Malaria	..	..	..	..	..	1(1)	..	..	1
Meningococcal Infection	2(1)	3	..	..	1	2	..	..	8
Ophthalmia	..	..	..	..	7	..	..	..	7
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	9(8)	1	4(1)	15(10)	..	..	..	..	29
Puerperal Fever	..	..	1(1)	..	..	..	..	..	1
Rubella	..	14(8)	..	..	10(6)	..	..	..	24
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	10(4)	81(57)	1	2(2)	1(1)	1	..	..	96
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	..	..	..	..	..	1
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	36(24)	6(2)	11(5)	10(9)	25(5)	2(1)	..	..	90
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	1	1	..	..	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Gynæcology and Obstetrics Refresher Course at the Women's Hospital.

A refresher course in gynæcology and obstetrics will be held at the Women's Hospital from August 31 to September 11. The course will consist of daily ward rounds conducted in groups, in which the routine work of the hospital will be demonstrated and taught, and of a series of demonstrations. Residence at the hospital during the period is advised and will be available. Tuition fees are £10 10s., payable to the Melbourne Permanent Post-Graduate Committee. The fee for residence, approximately £6 6s. per week, is payable to the hospital.

September Course at Mildura.

The following course at Mildura, which was omitted from the Committee's annual syllabus, will be held on September 19 and 20: Dr. J. H. Bolton, "Blood Dyscrasias"; Dr. B. Hudson, "Present Position of Cortisone and ACTH"; Mr. Murray Clarke, "Congenital Orthopædic Problems"; Mr. John Devine, "Indications and Contraindications in the Use of Intestinal Tubes".

Enrolments for this course should be made with Dr. P. G. Barker, Honorary Secretary, Mildura Hospital Clinical Society.

Inquiries.

Inquiries concerning all the above courses should be made with the Melbourne Permanent Post-Graduate Committee, 394 Albert Street, East Melbourne. Telephones: FB 2547, FB 2548.

SEMINARS AT THE ROYAL PRINCE ALFRED HOSPITAL.

THE following seminars, open to all members of the medical profession, will be held in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital, Sydney, on Fridays from 1.15 p.m. to 2.15 p.m. during the period July 3 to October 30, 1953:

July 3: Hæmatology Section, "Investigation of the Hæmorrhagic State". July 10: Cardiology Section, "Angiocardiography". July 17: Endocrinology and Metabolism Section, "Bacterial Metabolism with Relationship to Antibiotics". July 24: Thoracic Section, "Radiological Techniques in Thoracic Disease". July 31: Neurology Section, "Some Epileptic Equivalents". August 7: Gastro-Enterology Section, "Diverticula of Upper Gastro-Intestinal Tract". August 14: Thoracic Section, "Surgical Observations in Bronchial Carcinoma" (Dr. Gerbode). August 21: Hæmatology Section, "Myelofibrosis". August 28: Clinico-pathological conference. September 4: Endocrinology and Metabolism Section, "Recent Advances in Diabetic Treatment". September 11: Cardiology Section, "Review of Operative Results in Morbus Cæruleus". September 18: Neurology Section, "Vascular Anomalies of the Central Nervous System". September 25: Gastro-Enterology Section, "Diverticula of Lower Gastro-Intestinal Tract". October 2, Thoracic Section, "Impressions Abroad" (Dr. H. M. Rennie). October 9: Pædiatrics Section, subject to be announced later. October 16: No seminar. October 23: Cardiology Section, "Treatment of the Arrhythmias with Special Reference to Quinidine". October 30: No seminar.

Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Moffatt, Cathie Douglas, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1953), Belair, South Australia.

Moffatt, Jeannie May Douglas, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1953), Belair, South Australia.

Marshman, Ian, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1953), 41 Dequetteville Terrace, Kent Town, South Australia.

Tymons, Frances Teresa, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952), 20 Highbury Street, Prospect, South Australia.

Robertson, Thorburn Stirling Brailsford, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952), 14 Bice Street, Edwardstown, South Australia.

Deaths.

THE following deaths have been announced:

BULL.—Hilda Wager Bull, on June 29, 1953, at Hampton, Victoria.

WATKINS.—Arthur Moorehouse Watkins, on July 3, 1953, at Sydney.

DAY.—Edward James Day, on June 24, 1953, at Sydney.

Diary for the Month.

JULY 18.—Victorian Branch, B.M.A.: Country Branch Meeting.
JULY 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JULY 22.—Victorian Branch, B.M.A.: Council Meeting.
JULY 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
JULY 24.—Queensland Branch, B.M.A.: Council Meeting.
JULY 28.—New South Wales Branch, B.M.A.: Ethics Committee.
JULY 30.—New South Wales Branch, B.M.A.: Branch Meeting.
JULY 30.—South Australian Branch, B.M.A.: Scientific Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.